VOL. 32 JANUARY 1956 NO. 1

# BULLETIN

## OF THE NEW YORK ACADEMY OF MEDICINE

*Original Articles by*

ALBERT I. LANSING, Ph.D.

ROSS A. McFARLAND, Ph.D., Sc.D.

HERBERT PARSONS

PREVENTIVE USE OF PSYCHOTHERAPY IN CHILDHOOD

*Transcription of a Panel Meeting*

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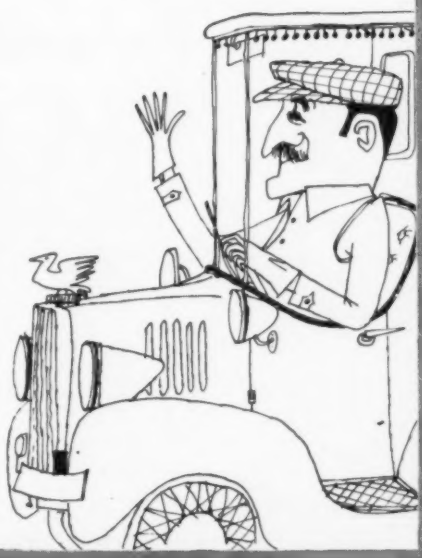

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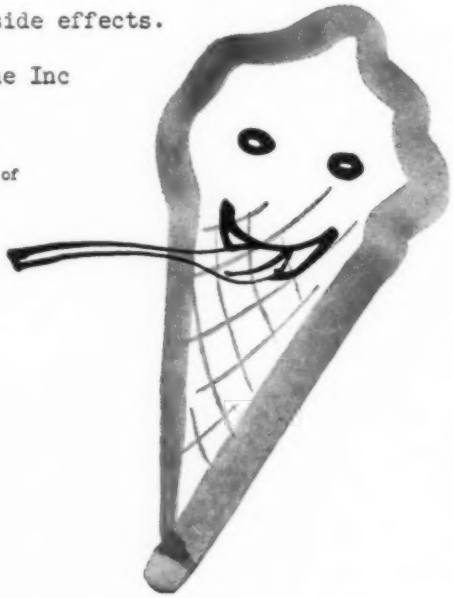

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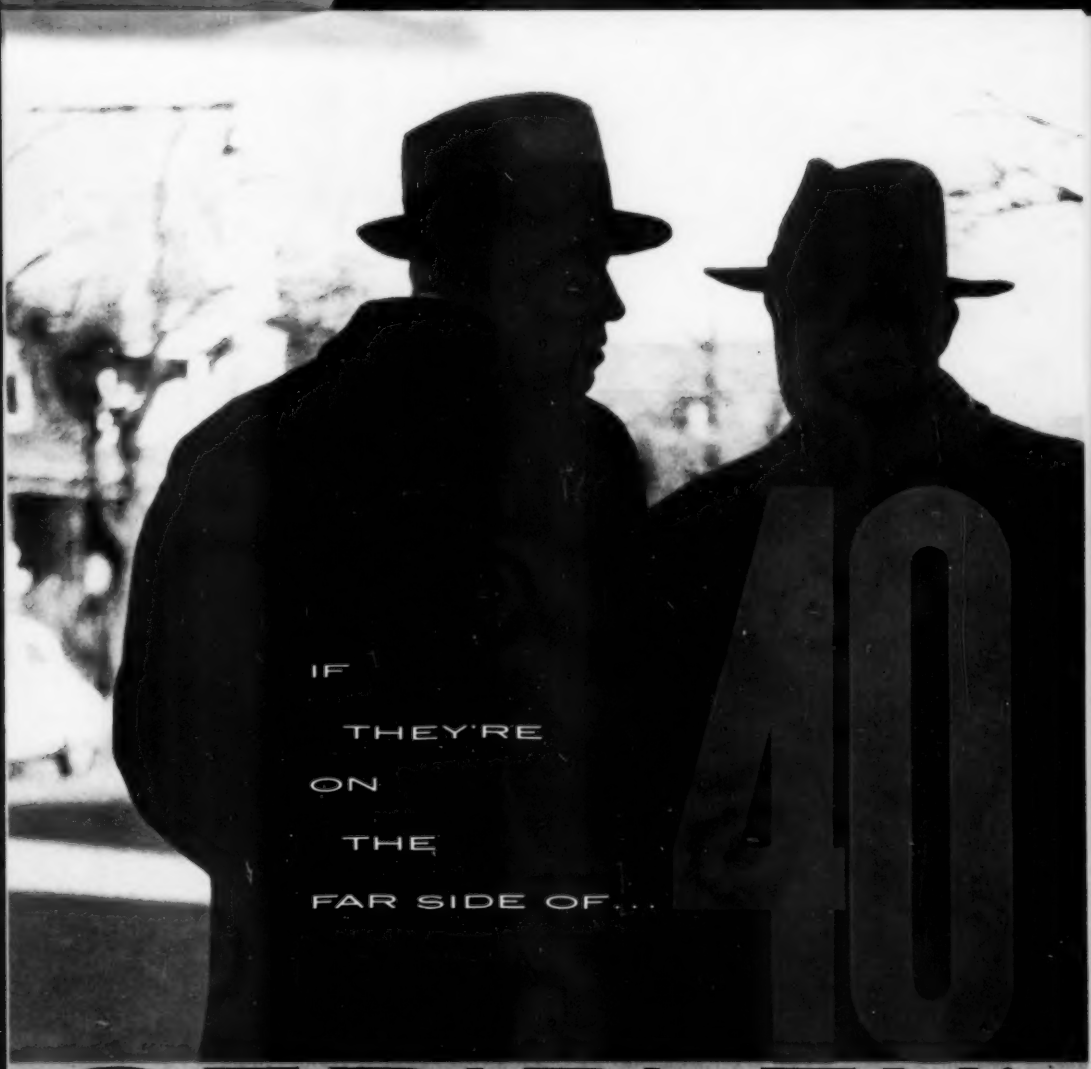


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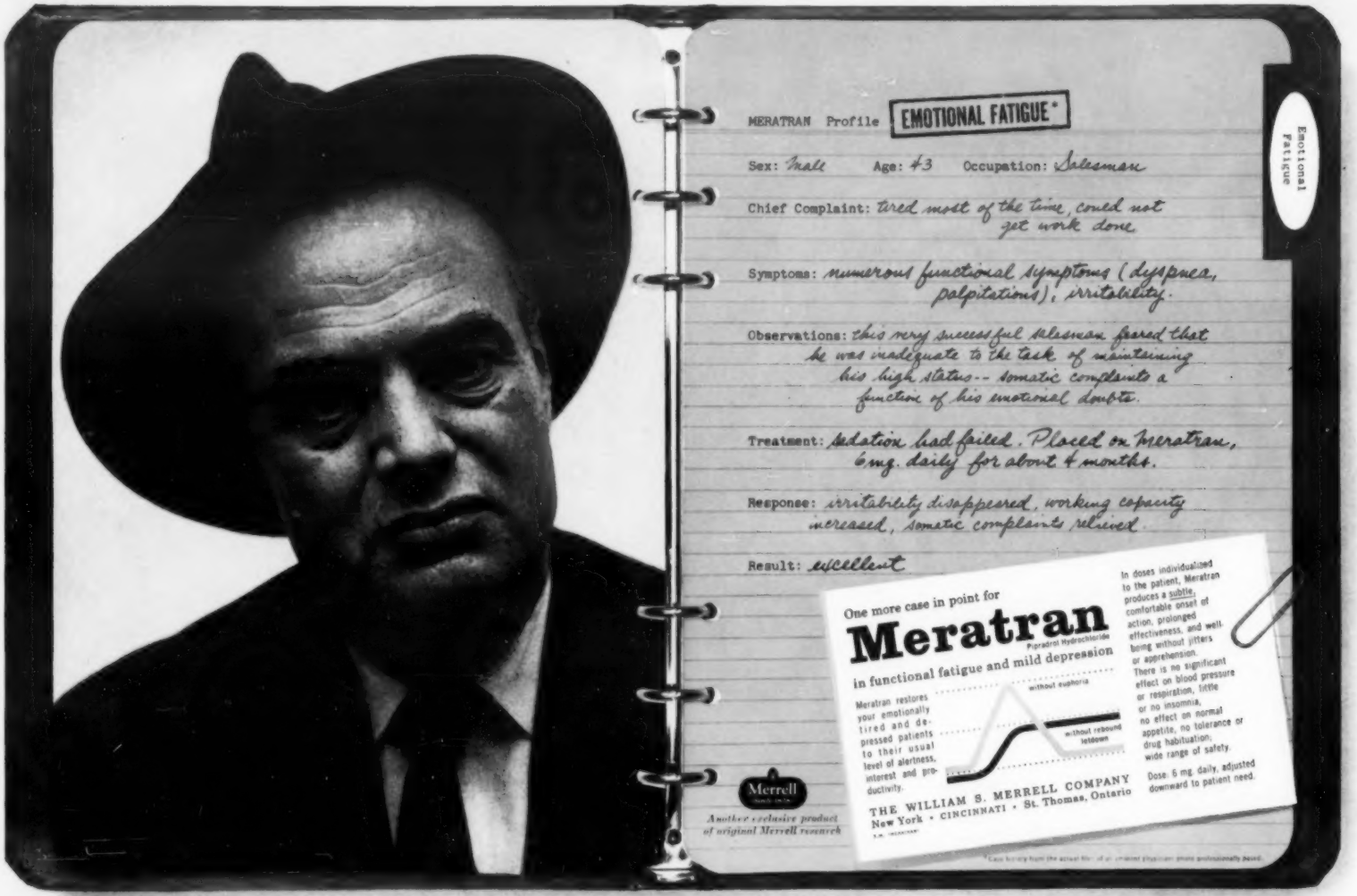
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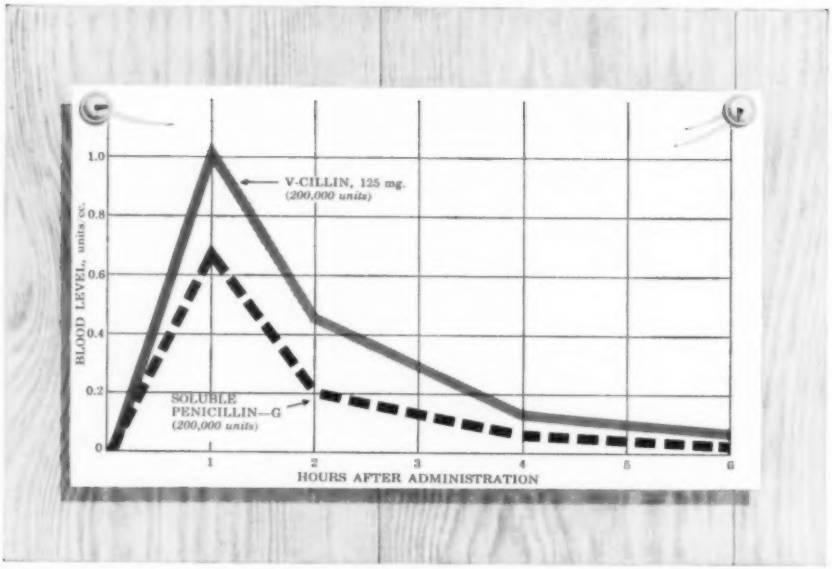


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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 32, NO. 1 JANUARY 1956

# OPENING ADDRESS*

## *Twenty-Eighth Annual Graduate Fortnight*

EDWARD J. DONOVAN

President, The New York Academy of Medicine

As President of The New York Academy of Medicine it is my great pleasure to extend a most cordial welcome to you at this opening meeting of our Twenty-Eighth Graduate Fortnight.

For the benefit of those who are with us for the first time this evening, I would like to review briefly the origin of the Graduate Fortnight and call your attention to a few important features of the program.

The Graduate Fortnight was actually started at the suggestion of Dr. Ludwig Kast in 1927. He was then Professor of Medicine at Post-Graduate Hospital and Medical School and had been interested for many years in graduate training of physicians. The plan of having a two-week seminar on various subjects in the postgraduate fields of medicine and surgery was greeted with enthusiasm. Some of the most distinguished names in medicine and its allied sciences have participated in these meetings since their inception in 1928 and they have become

* Presented October 10, 1955, at The New York Academy of Medicine.

an integral part of the Academy's activities reaching large audiences, who look forward to them each year.

The title of this year's program, PROBLEMS OF AGING, is surely one of the most timely, and it is extremely interesting to note, that this was also the title and subject of the first Fortnight held in 1928. It is now an established fact that we have a growing proportion of our populace living beyond the age of sixty-five years and as these numbers increase there is bound to be a corresponding rise in the incidence of chronic and geriatric diseases and a relative need for major surgery in these older patients. The problems of aging are too numerous for us to mention here but the program committee has gone into this topic in great detail and we will hear much more about it at the various discussions and clinics during this Fortnight. The program, as you will notice, now includes three very important memorial lectures, i.e., the Ludwig Kast, the Wesley M. Carpenter and the Harlow Brooks.

There is little doubt that you will all realize as you scan this year's program that its arrangement was a stupendous task which was started last December. I would like to take this opportunity to thank all those who helped make it possible: Dr. Irving Wright, Chairman of the Committee on Medical Education, Dr. Robert Craig, Executive Secretary, and the members of this committee. Dr. Clarence de la Chapelle, Chairman of the Subcommittee on the Graduate Fortnight and the sixteen members of his committee deserve great praise for spending many hours of hard work in arranging this program. I would also like to thank Dr. Charles Wilkinson, Jr., Chairman of the Committee on Panel Meetings and the nine members of his committee, as well as the Directors of the Scientific Exhibit, Dr. Alfred Angrist and Dr. Norman Higinbotham. Please do not miss seeing this interesting exhibit. We are very grateful to Dr. Carl Muschenheim, Chairman of the Committee on Hospital Clinics and the members of his Committee who have arranged a splendid group of clinics. These are held in the various hospitals each afternoon and I urge you all to visit them as you will find them well worth your while.

I am confident that the work and effort put into the arrangements for this program will bring rich rewards and I hope you will all enjoy this Graduate Fortnight meeting.

# WHAT IS AGING?*

## *The Ludwig Kast Lecture*†

ALBERT I. LANSING, Ph. D.

Professor of Anatomy, Emory University School of Medicine, Emory University, Georgia

To be called upon to deliver this lecture honoring Dr. Ludwig Kast is of particular significance to me. Dr. Kast was a forward thinking man, who, through the Josiah Macy, Jr. Foundation, did much to further the development of research on aging in the United States: This is a matter of record. It is also a matter of record that my first post-doctoral post in 1941 at the Washington University School of Medicine was financed by a grant for research on aging from the Josiah Macy, Jr. Foundation.

One might assume, from the title of my talk, that a firm definition of aging will be offered before I close; the assumption, unfortunately, would not be valid. According to my desk dictionary, "to define" is:

"1. To mark the limits or boundaries of; to make distinct or fix in outline or character.

2. To describe, expound, or interpret; to explain, hence, to determine the precise significance of; to discover and set forth the meaning of, as a word.

3. To set apart in a class by identifying marks; to distinguish."

Any number of maladies of man or beast can be defined in accord with the preceding criteria: diphtheria, poliomyelitis, erythroblastosis, etc. Diphtheria, for example, is defined as:

> "An acute infectious disease or toxicosis due to the presence of *Corynebacterium diphtheriae*. The disease may be attended with patches of false membrane in the throat or on other mucous surfaces and the resulting absorption of diphtheria toxin. The disease is attended with swelling of the larynx and pharynx, and consequent dyspnea, aphonia, and dysphagia. The general symptoms are: fever, heart weakness, anemia, and great prostra-

* Presented at the 28th Graduate Fortnight on *Problems of Aging*, of The New York Academy of Medicine, October 10, 1955.

† In honor of Dr. Ludwig Kast who first suggested the Graduate Fortnight.

tion. Diphtheria continues from a few days to one or two weeks, frequently ending fatally. It is extremely contagious."

This is a definition. The disease is delimited and set apart by identifying marks. A specific causative agent is indicated, the symptoms are listed, as is the time course and prognosis.

How can we do the same for aging? What is the causative agent? When does the condition begin? What are the changes that occur in aging? What is the time course of the disease (if, indeed, aging may be called a disease)? The only point that may be made with assurance is that aging invariably results in death of the organism.

From a less academic viewpoint, the situation is even further confused by a lack of resolution between concern with aging and concern for the aged. The last ten years have seen a phenomenal growth of interest in problems of the aged. Thousands are professionally concerned with the welfare of the elderly and the senile. With the tremendous increase in life expectancy that we are enjoying today and is mushrooming steadily, our entire population structure stands to be altered sharply. Thanks to the conquest of infectious diseases more of us are living long enough to experience cardiovascular diseases, malignancies and senile decay. Medicine is increasingly concerned with problems attending care of the aged patient.

With more of us living long enough to enter into post-compulsory retirement life, there is ever-growing concern by social scientists and economists in annuities, retirement schemes and Social Security systems. Still others press for extension of retirement age or abolition of compulsory retirement. Entry into retirement usually signifies the beginning of a period of intense insecurity. Finances are inadequate; modern transport has spread families over hundreds and thousands of miles so that the retired person or couple cannot readily move in with children. Even if the children do live nearby, modern housing is not designed to accommodate the presence of old folks in a dwelling. The feeling of being un-needed and unwanted grows. It is into this breach that the social workers attempt to step.

All of these problems that have been listed are real and severe, but they are problems of the aged. When it comes to problems of aging, the strategic rather tactical problem, the academic issue, the questions of what is aging, why is aging, what are the changes that occur during aging, it is painful to note that there are less than a handful of serious

workers in this field in the United States.

There are probably a number of factors responsible for the paucity of basic scientists in research on aging. Funds for research are more readily available for research on diseases of popular concern, but I do not believe that there is a serious shortage of funds for research on aging. More likely than not, the lack of clues that might direct research into specific avenues is primarily responsible. An appreciation of the apparent inevitability of aging no doubt dissuades many from dabbling in this problem.

I have already taken the view that a sound definition cannot be formulated now. It may also be noted that there is a surprising lack of variety insofar as theories of aging are concerned. Let us omit from our discussion the frankly irresponsible and imaginative notions that crop up from time to time, the "fountain of youth" sort of thing. Not much will be missed if, in addition, we omit discussion of the theory of auto-intoxication resulting from intestinal putrefaction. Metchnikoff[1] was seriously taken by this notion at the turn of the century, and although it more or less faded after Metchnikoff's death, every now and then a paper appears urging that intestinal putrefaction is the cause of aging. The same objection that applies to the theories that aging results from failure of the cardiovascular system, or nervous system, or failure of any particular mammalian organ, also applies to the intestinal intoxication theory. I have stressed repeatedly, and will continue to stress, that aging is too fundamental a process to be rationalized so simply. Aging is virtually universal. It occurs in plants as well as in animals. It occurs in animals without arteries, without large intestines, and without complex nervous systems. Even in these relatively simple animals the process of aging follows a pattern much like that of man. The organism develops, goes through a brief adolescence, matures, enjoys a brief period of adult vigor, gradually declines, and dies.

To be taken seriously is the concept that senescence is due to the failure, or deterioration with time, of the protoplasmic colloids. Among the early proponents of this theory were Dhar and Marinesco. A parallel is drawn between the *in vitro* aging of colloids as manifested by syneresis, and the apparent loss of water from *in vivo* colloid systems. Similar in principle, but put more simply, is the often expressed thought that aging is like the running down of a clock, the wearing out of an automobile part or a pair of shoes. The difficulty with this whole con-

cept is that the living cell is not a clock, not an automobile motor, nor a pair of shoes. The latter are non-living systems—they do not possess a self-synthetic mechanism. The living cell does. A critical, diagnostic feature of the living system is the capacity for self-renewal. It is an expression of this capacity for self-renewal that is measured in turnover studies with radioactive isotopes. Protoplasmic constituents are constantly being replaced albeit at varying rates. If, in senescence, there are "old" protoplasmic constituents present, it can only be due to inadequacy of the self-synthetic mechanism. Indeed, it is not too far-fetched to speculate that aging is primarily due to an insufficient rate of protoplasmic self-duplication.

One last general group of theories on aging remains to be considered. Although they vary in detail, all hold in principle that in senescence there is a progressive accumulation of toxic materials in the cell. These materials, whether they are held to be pigments, crystals, insoluble compounds, or products of incomplete metabolism, are supposed to interfere with vigorous cellular life. Some decades ago, Benedict refined this concept by proposing that in senescence cellular permeability is decreased. More recently, I espoused this idea and elaborated it still further by proposing that the decrease in cell permeability is a product of an increase in the calcium content of the cell surface.[2] Aside from the fact that there is little evidence that cell permeability does decrease with age, these theories leave us in much the same quandary as we would be without them. Why should permeability of the cell decrease with age? Or, if calcium does increase with age to decrease transport across the cell membrane, why should this happen? One is taken back to my earlier suggestion that aging may involve inadequate self-duplication, in this case referring specifically to inadequate renewal of the cell surface.

Thus far I have emphasized the things that we don't know. Perhaps I have been too gloomy. There are some observations that could well serve as take-off points for further experimentation.

First, I have in mind a relatively uncommon clinical situation known as progeria. In this disease of children there is the appearance of many of the superficial characteristics of senility. Although abnormal adrenal and anterior pituitary glands in the victims of progeria might point to an endocrine disturbance, the suggestion of premature senility is strong. As a matter of fact, many of these children die of coronary thrombosis. It may well be that the association between progeria and senility may be

little more than a figment of the imagination. On a long chance it may also be that a profound metabolic disturbance does bring about premature senility in these children. A comprehensive analysis of the clinical and histological changes in such individuals might be rewarding.

Returning to tissues and cells one comes to the liver, the happy hunting ground of biochemists and histologists. There have been a few studies of the nucleic acid content of young and old liver cells. One might expect a quantitative reduction in either or both pentose and desoxypentose nucleic acid in old cells. Nucleic acids are thoroughly established as associated with protein synthesis. Old tissues presumably are less capable of protein synthesis and, hence, should contain less of these materials. However, Lowry[3] and, later, Schulz[4] found no significant change with age in the amount of either of the two nucleic acids. It may well be that the methods employed were not sufficiently subtle to detect fine differences or it may well be that the physical structure of the nucleoproteins change with age rather than their amount per cell. Certainly, the old liver cell is not as effective as the young. Mitotic activity in regenerating old liver is lower than that of young liver. Also, the $P^{32}$ uptake of old liver after experimental hepatectomy is reduced. McKellar's[5] cytological analysis of rat liver is also interesting. During fetal life there is, of course, a high level of mitotic activity. This means that both chromosomes and nucleus are dividing along with the cytoplasm. Later, in the young animal one finds an increasing number of binucleate cells along with the products of normal mitosis. In this situation it would appear that while the chromosomes and nuclei are dividing in synchrony, the cytoplasm is not. Still later, in middle life polyploid cells increase in population density, indicating that while chromosomes are multiplying both the nucleus and cytoplasm are lagging. This progressive failure of capacity for multiplication may be taken as a measure of reduced growth potential.

*This* is my thesis—aging is a product of reduced growth potential. It is a restatement of my earlier suggestion that aging must be a consequence of inhibited capacity for self-duplication. There is evidence to support this view. Nothing would please me more than to review these data in detail. Yet, out of consideration for my audience I will be most concise. Biologists studying senescence are few and the data are slow in accumulating. One is compelled, as I have been, to cite the same works over and over again.

Chronologically, Sonneborn's[6] experiments of 1930 come first. Although he was not particularly interested in gerontology at the time, his observation on the flatworm, Stenostomum incaudatum, represents one of the major advances in the field. His experimental animal, Stenostomum, was presumably genetically homozygous and was raised under standardized conditions. Reproducing asexually, Stenostomum multiplies by transverse fission to give rise to anterior and posterior daughter organisms. These two differ in one significant respect; the anterior product receives the head and much of the trunk of the dividing mother and has only to regenerate the tail component to be complete, while the posterior product of transverse fission must regenerate a full head and much of the trunk.

Thus, the anterior daughter experiences little cell multiplication and growth while the converse is true for the posterior daughter. In the design of his experiment, Sonneborn segregated these fission products in isolation cultures and established two contrasting lines of purely anterior or posterior products through a series of generations. Bearing in mind that all the lines were genetically uniform and nurtured under standardized environmental conditions, one might expect comparable life spans for all of the lines. This was not the case. The mean length of life in days for all of the anterior lines studied was $35.0 \pm 1.1$, while four posterior lines had a mean life span of 63.5 days, two lived 77.0 days and the last two lines had lived 115.0 days, at which time the lines were discarded. It would appear that lack of active growth in the anterior lines is coupled with the observed reduced longevity.

Several years ago, I made a comparable series of observations on a multicellular but microscopic fresh water organism, the rotifer.[7] The rotifer's development is determinate; all of its cells are formed during embryonic life and, hence, are of the same age. In addition, since its reproduction is parthenogenetic, all the reproductive products of an individual are genetically identical. Using a standardized culturing technique, I attempted to determine if the progeny of actively growing, adolescent rotifers have different life spans than progeny of full grown and elderly mothers.

As in Sonneborn's experiments, two types of divergent lines were established. One was composed of successive generations of first born rotifers; the other consisted of successive generations of descendants of full grown or elderly mothers. In the lines of rotifers derived from

adult mothers the mean life span decreased in each successive generation until the line became extinct, and the number of generations required to bring a line to its end depended upon the age of the mothers. Lines derived from elderly mothers died out in four generations, from middle-aged mothers died out in eight generations, and from newly matured mothers in seventeen generations. Apparently a capacity for reducing longevity is transmitted through adult rotifer eggs. This does not occur in lines of rotifers from actively growing adolescent animals. Longevity of each successive generation is greater than that of the preceding, so that in experiments carried through 54 generations rotifers were developed whose longevity was four times greater than that of the original stock. The eggs of actively growing rotifers do not contain, or at least do not express, the capacity for reducing longevity. There were a number of interesting ramifications to these experiments, but they are not essential for this discussion. One intriguing question does come up. How does one reconcile these observations with Weismann's concept of the immortality of germ-plasm? If our observations are sound, it would appear that the germ-plasm of the adult of at least one species is as mortal as its somatoplasm. Perhaps the concept should be modified to this extent; the germ-plasm of only the actively growing young individual is potentially immortal and perpetuates the species. It may even be that aging of a species results from conditions favoring breeding of adult and elderly individuals.

We still have not defined aging. Can we at least develop a reasonable description of the process? Aging certainly is not advantageous from the point of view of the individual, it always has a fatal outcome, time is of the essence. Lastly, aging occurs when growth slows down or stops.

Aging, then, is a process of unfavorable progressive change, usually correlated with the passage of time, becoming apparent after maturity, and terminating invariably in death of the individual.

It is interesting to note that the situation today in regard to a concept of aging is not too different from what it was 30 years ago. Dr. Raymond Pearl,[8] in his excellent little monograph entitled, *The Biology of Death*, summarized his thinking in this way:

"The problem of natural death has two aspects, one general, the other special. These may be stated in this way:

1. "Why do living things die? What is the meaning of death in the general philosophy of biology?

2. "Why do living things die *when* they do? What factors determine the duration of life in general and in particular, and what is the relative influence of each of these factors in producing the observed result?"

These two questions are fundamentally the same questions with which we are concerned today. Dr. Pearl goes on to list five biological generalizations concerning natural death, which again I will quote.

A. "There is an enormous variation in the duration of life, both intra and inter racially."

B. "There is no generally valid, orderly relationship between the average duration of life of the individuals composing a species and any other broad fact now known in their life history, or their structure, or their physiology." (He refers here to the usual attempts at correlation between metabolic rate and longevity, duration of fetal life and longevity, etc.)

C. "Natural death as distinguished from accidental death is preceded by definite structural and functional changes in the body." (We agree that there must be at least some structural and functional changes in aging but in essence we have failed to characterize them.)

D. "Natural death occurs normally and necessarily only in animals composed of many cells." (This statement is probably true in a qualified sense only. We now know that at least some Protozoa do age and die in the absence of periodical nuclear reorganization.)

E. "Life itself is a continuum. Natural death is a new thing which has appeared in the course of evolution. The somatic death of higher multicellular organisms is simply the price they pay for the privilege of enjoying those higher specializations of structure and function which have been added on as a side line to the main business of living things, which is to pass on in unbroken continuity the never-dimmed fire of life itself."

This was the status of affairs 30 years ago. It is remarkably unchanged. What I have tried to do is to draw a sharp line between problems of the aged and problems of the aging. Because of the rapid changes occurring in our population structure, we are urgently concerned with issues involving clinical management of the senile, social and economic ills of the elderly. The biology of aging—the study of the mechanism of aging is lagging seriously. Yet, in the long run, I strongly suspect that much of what we can do in at least the clinical care of the elderly will depend upon developments at the biological level. As Dr. Robert Moore

has aptly put it: "The biology of today is the medicine of tomorrow." This might be paraphrased to read, "The biological research on aging of today is the geriatrics of tomorrow."

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# THE PSYCHOLOGICAL ASPECTS OF AGING*

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## Introduction

In the current literature on the medical aspects of aging there seems to be an increasing emphasis on the incidence of disease and disability among older people and on the ways in which such changes might be prevented. In a somewhat similar fashion the reviews of the physiological aspects of aging stress the gradual impairment of various organic functions and the loss of capacities.[1] In contrast to these trends, the experimental literature in the field of psychology tends to bring out the fact that many abilities are maintained through a much longer period of the life span than previously expected. In fact, actual improvement can be demonstrated, especially in those functions which are of greatest importance in daily living. The primary objective of this paper is to examine the experimental findings which might aid the physician in his daily practice.

As a general orientation to the following discussion on the psychological aspects of aging, it is in order to present certain general concepts which will influence the interpretation of the specific findings. In the first place, it is important to realize that there are great differences in the inherent abilities or capacities of individuals of any given age. When any psychological trait is measured in groups which differ in age, numerous members of the oldest group will perform more effectively than the average of the youngest group, and many in the youngest group will be below the average in the oldest group. Chronological age alone, therefore, is a very uncertain indication of functional ability. Hence a concept of functional rather than chronological age is required.[2, 3]

At present, most of the information available in regard to aging is

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in terms of group averages. Such values obscure the variation at any one age. A significant assessment of functional age requires that individuals be evaluated against themselves as well, i.e., in terms of the history of the processes under question within the individual as well as in groups. The implications of this for the health status of older people are that the relationships between behavior and physiological status are not very close, and a wide latitude of possible adjustments should be assumed. Age in itself should not be considered detrimental. Every physician is aware that a physical impairment in one patient may produce invalidism whereas another patient with a similar disability may make a satisfactory adjustment.[1]

A second consideration relates to the increase in longevity which has been achieved and the implications of aging on vocational fitness. It is important to know the nature of the changes which occur in sensory and motor skills and in mental adjustment, and what effect these changes will have on employability. The view to be presented here is that such changes cannot be arbitrarily evaluated as good or bad, but rather that they must be clearly understood in relation to the demands of specific jobs or employment possibilities. Prolongation of life may well involve a comparable extension of time in various abilities, as well as an extension of the capacity to accept economic and social responsibilities.

The physician can make an outstanding contribution in preserving the useful lives of older workers and utilizing fully their skill and experience. This requires a continuous adjustment between the capacities of older individuals and the requirements of their vocation. The reclassification of older workers to jobs where they can perform efficiently and safely, and the re-design of jobs so that age changes are of minor importance should be based on a knowledge of the capacities of the individual in relation to the critical psychological requirements of the job.

A third basic consideration is that older people with adequate motivation can learn new activities and continuously readjust to the changes which may occur with age. The development and maintenance of adequate motivation will overcome the dissatisfactions which older people may experience, largely as a result of anxiety over health and economic status and the feelings of rejection which they experience as a result of our social environment. Thus the recommendation that older people

should maintain a variety of interests, accept the changes which occur with age, and recognize the importance of participation in community activities has adequate foundation in controlled psychological study.

Finally, the role of the average physician in the field of aging should be one of anticipating the general and special problems of each patient at about 50 years of age rather than at 70. This applies to mental and emotional problems as well as to physical disabilities. Just as the engineer at his drawing board should foresee defects in equipment before it is built, and give careful instructions in regard to its use, so the physician should detect and instruct his patient in regard to psychological and organic tendencies to disease at an early age, or at the latest by middle age. It has been my good fortune to work with physicians in a longitudinal study of selected professional groups (problem medical cases) through a period of 15 to 20 years. The findings are revealing in regard to the importance of preventive medicine.[2] Many case histories could be cited of the prolongation of the active careers of persons who, without preventive medical advice, might have been retired much earlier.

An attempt will now be made to analyze and interpret some of the changes which occur with aging in regard to sensory, motor, mental, and emotional functions. These findings will then be appraised in relation to the vocational and social adjustment of older persons.

## The Influence of Aging on Sensory Functions

With aging, all of the senses manifest changes to some degree or extent. In such functions as smell, taste, vibratory sensation, and pain, the changes are usually of little significance, and may even be advantageous in certain tasks. In other areas, such as vision and hearing, the changes are often not extensive, and frequently cause less interference with adjustment or industrial productivity than is generally supposed. In some occupations, however, adequate vision and hearing are of special importance, and even small changes must be taken into consideration, especially in the presence of pre-existing handicaps.

*Vision:* Certain of the changes which occur with age in the visual functions are well known. The loss of elasticity in the lens, resulting in a narrower range of accommodation, is gradual, beginning even in childhood. The practical importance of this change is usually not very great, since adequate correction by lenses is feasible. It has also been well recognized that a gradual decline in visual acuity for distant

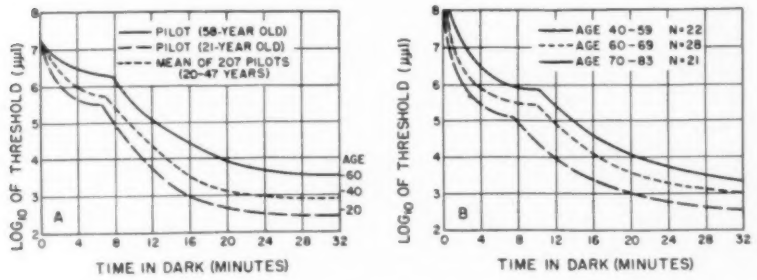


Figure 1. The relation of age to thresholds for dark adaptation. The figure on the left is based on 207 airline pilots (A). The figure on the right (B) comes from a study using subjects from the general population. The data indicate that complete dark adaptation, as represented by the lowest intensity of illumination at which an object can be seen, decreases significantly with age. (Reprinted by permission from *Human factors in air transportation*, by McFarland, R. A.[5] Copyright 1953. McGraw-Hill Book Company, Inc.)

objects also takes place, becoming evident on the average after about age 40.[2, 4]

Alterations with age in other visual functions have also been reported, but the investigations have not been very extensive. Apparently the range of the visual field becomes somewhat narrower, and the perception of depth and of colors may become less accurate. The available data in these respects, however, do not permit the construction of age curves.[4]

A change which may have considerable practical significance is the decline of night vision with age which occurs as a progressive loss of sensitivity to dim light under conditions of low illumination. The rise in visual thresholds with age has been amply demonstrated[3, 5] (see Figure 1). Recently we have made a study of this phenomenon under carefully controlled experimental conditions (see Figure 2). A correlation of 0.895 was obtained between age and the dark-adapted threshold, an unusually high relationship. In practical terms, this finding indicates that for a light to be just seen by an eye used to the dark, each increase of 13 years in age requires a doubling of the intensity of the light. Such facts may help to explain the difficulties persons over 55 or 60 may experience in driving or flying at night, and may also be related to the age-change in visual acuity already mentioned.[6] If an elderly man drives an automobile with a tinted windshield, it is as if an optical wedge were

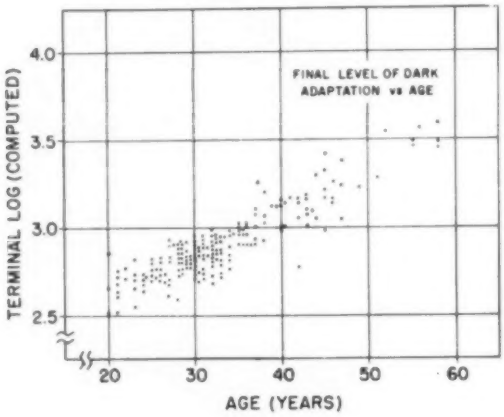


Figure 2. Scattergram showing the relationships between final level of dark adaptation and age. The correlation computed from these data was 0.895, and the loss of sensitivity in dim illumination with increasing age is striking. The final level of adaptation reached is represented in Figure 1, shown earlier, as the end-points of the adaptation curve after 32 minutes in the dark. (From McFarland, R. A. and Fisher, M. B.,[5] in *Journal of Gerontology* 10:424-28, 1955. Reprinted by permission.)

before him, reducing the amount of light transmitted and thus adding to the limitation due to his age.

*Hearing:* With increasing age, the change in hearing in the average person is a well-recognized phenomenon. In general there is a definite but relatively small decrease in sensitivity, chiefly confined to the upper frequencies, i.e., 2,000 cps and over. In a group of subjects chosen to represent a cross section of the population between 20 and 60 years of age, no significant deterioration with age was observed in the audiograms below 2,048 cps. Above this critical frequency, the loss became appreciable. The median loss above 4,096 cps was about 30 db for those from 40 to 60 years of age[2, 4] (see Figure 3).

The practical implications of the loss of auditory acuity that occurs with age relate chiefly to the effect upon conversation and communication, save for occasional occupational requirements for hearing certain high frequency sounds. Consonants, particularly, will be less distinguishable, and the use of prosthetic devices to amplify the higher frequencies may be required to enable older persons to participate freely in conversation and social interchange. The partially deaf old man is not so

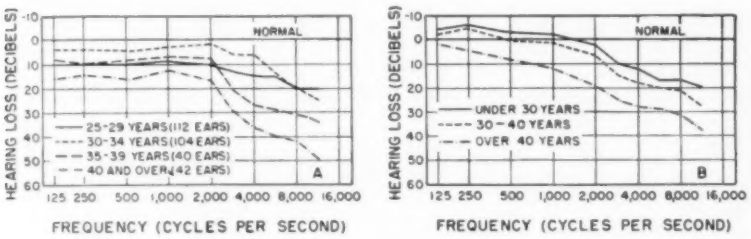


Figure 3. The relation of age to auditory sensitivity in airline pilots. Mean audiograms of 200 PAA and UAL pilots (A) and 449 AA pilots (B) indicate that their auditory sensitivity declines slowly with age, especially for the higher frequencies. (Reprinted by permission from *Human factors in air transportation*, by McFarland, R. A.[3] Copyright 1953. McGraw-Hill Book Company, Inc.)

much a problem as the partially deaf old man who will not wear his hearing aid. Moreover, the older person experiences relatively less difficulty in hearing in the presence of background noise, since there is less masking by the other sounds than is the case with normal hearing.

It is interesting to translate these findings into the vocational situation, as in airline pilots. The regulatory agencies in the field of transportation at one time considered a new hearing standard which would have grounded many of the pilots. We came to the rescue of the older pilots by pointing out why some leniency should be permitted: older men with hearing losses tend to have more normal responses in the presence of aircraft noise. This is a result of the "recruitment" phenomenon. Exposed to a noise of 40 db, one deaf pilot's hearing loss was reduced to 25 db; masked with a noise of 60 db, his loss was only 15 db; and in a noise of 80 db, his hearing was normal. The basis for this phenomenon is difficult to explain, but one reason may be that low-intensity signals are masked. In fact, for loud intensities the person with marked hearing losses, as measured by an audiometer, may actually hear quite well. Older pilots with hearing losses therefore should be tested in simulated aircraft noise. If the hearing losses do not interfere with the intelligibility of normal conversation or with aircraft signals in flight, safety will not be compromised.[2] The proposed new hearing standards were altered after the results of our studies were presented. Close cooperation was obtained from the union when the members sincerely believed that we were interested in prolonging their useful flying careers.

It is important to interpret the implications of aging in any sensory field in relation to vocational adjustments. Experience in this field requires a constant revision of our earlier and possibly erroneous concepts. Flying an airplane was originally believed to be an avocation or vocation of young men. It may be surprising to many to learn that there are over 1,000 private pilots over 60 who hold medical certificates with the Civil Aeronautics Administration. In 1954 there were more than 300 airmen 50 or over, holding medical certificates as air transport pilots, and about 50 approaching 60 years of age.[2, 3] It would have been unwise to ground such individuals for sensory defects, since their operating record has proved excellent. The important point is that age changes vary greatly from one person to another, both in nature and extent. An appraisal of a person's capabilities at any given period should include the amount of compensation present, based on previous experience. It is well known that compensation for declining functions can and usually does occur, so that the end results of behavior often show little change, and sometimes even improvement. It thus becomes of great importance to establish when, in the normal process of aging, deterioration is no longer compensated by prosthetic aids, past experience, or a change in methods.[3]

## The Influence of Aging on Psychomotor Functions and Skill

Extensive studies of motor activity have revealed no sudden alterations in the speed of response from one age group to another. There is a gradual rise in quickness of response in childhood and youth, followed by a slow decline in maturity. However, individual differences at any age are great, and the average performance of a considerable number of older persons equals or exceeds that of individuals who are several decades younger.[7]

Driving an automobile is a good example of a complex skill that involves factors other than reaction-time. Three of its essential elements are steering coordination, braking reaction-time, and sensitivity to glare. After 30 to 35 years, each of these shows a general decrease in ability with age. It is noteworthy that the most complex skill, which requires a high degree of eye-hand coordination—steering coordination—declines more slowly than either glare vision or braking reaction-time. This difference may be interpreted as showing that decline in skill may be retarded by an age-experience factor. If ratings on several measures of

driving ability are combined for a composite "good driving" score, a general increase in competency with age is usually apparent.[8] There is no evidence that older persons are greater accident-risks than younger ones in any form of transportation. In fact, the reverse is often the case.[2, 9, 10]

In the comprehensive study of aging at Cambridge University, England, deterioration in psychomotor skills and mental functions has been interpreted in terms of central nervous system *receptor* mechanisms. In new situations the mechanisms concerned with organizing verbal or visual material operate less efficiently in the older person and require stronger "signals", or more time, to relate the new data to relevant material in past experience. Such changes may appear as early as 35 or 40 years of age.[11] If older persons are allowed to deal leisurely with incoming problems, there is less likelihood of their becoming "muddled." They should not be placed on jobs requiring continuous rapid action, but they are particularly well suited for operations which demand a high degree of accuracy, since their deficiency in organizing new material is often more than offset by gains in quality and accuracy of performance once the material is assimilated. This has important implications for driving an automobile, flying an airplane, and many skilled tasks in industry.

## The Influence of Aging on Mental Functions

Mental ability is based on memory, learning, imagination, and thinking, and they are all facets of more general capacity. It is not surprising, therefore, that in senile subjects profound changes in such functions as memory or learning are accompanied by alterations in other psychological reactions. Several studies have been made to compare *mental tests* in adolescence, maturity, and late maturity, in normal subjects. The results of three such investigations are presented in Figure 4. The curves agree in showing rapid gains during adolescence, with a peak around the age of 20 years, followed by a gradual decline. Although the individual differences were large for all ages, the general trends were similar in all studies.[12, 13] Such tests involve time limits, and this tends to penalize the older person for the reasons mentioned earlier.

The more complex a function becomes psychologically, i.e., the more it depends on experience, judgment, and reasoning, the more resistant it is to deterioration with age. For instance, in a study of vocabu-

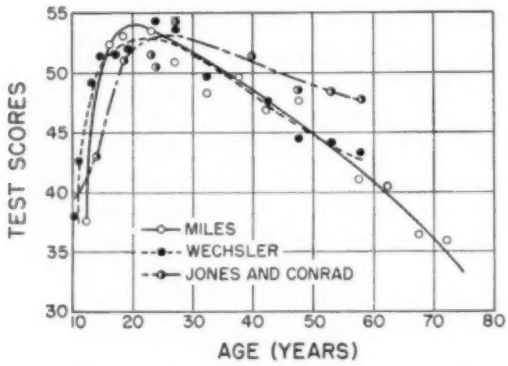


Figure 4. The influence of age on intelligence test scores. The curves, comparing results from three different intelligence tests, show that the mental functions measured by the tests increase up to 20 to 25 years and then show a gradul decline. (Data from Anastasi and Foley, ref. 13 and from Kaplan, ref. 12.)

lary it was shown that professional persons progressively increased in ability through the ages of 60-70 years. Subjects who were institutionalized, however, where language was not a major factor in daily living, showed an opposite trend.[14] Apparently the brain, like other organs of the body, shows continuous improvement over the life-span if appropriately "exercised."

In an extensive study of adult learning at Columbia University, large groups of subjects at various age-levels were given a wide range of tasks, varying from learning to typewrite, or to drive a car, to the retention of complex logical material. In general, the ability to learn showed a definite rise up to 25 years, after which it began to decline slowly. The authors concluded that no one under 45 should refrain from trying to learn a new task because of fear of being too old to be able to learn it.[15] Recent evidence would indicate age 50 or 55 as a more appropriate figure. The inability of an adult to learn may be caused by an original lack of mental capacity, or by factors other than age. For example, the desire or necessity for mastering a given problem may not be great enough to evoke the effort required for its solution. On the other hand, motivation may be good; but either old habits, or such traits as fear of ridicule, may interfere with the learning processes. In general, the greatest difficulty may be expected when the learning

of the new material requires the "unlearning" of previously established patterns.

Another change in advancing years is the decreasing ability to take in new material quickly and remember it over short periods of time. This fact was verified in a recent study of the capacity for immediate memory in 174 older subjects in comparison with an equal number of men in their twenties. The two groups were of equal intelligence, as judged by mental tests. The results showed that the older persons were slower than the younger ones in their ability to form new associations based upon entirely new material.[16] Although it may be true that an average memory score is poorer at 65 than at 50 years, it is not known whether a loss in memory-ability during this period consists of a small loss experienced by many or of a great loss suffered by a few.

Insight for meanings, critical judgment, and standards of excellence are not affected unduly until the latter decades. Intelligence tests that are intended to measure innate mental capacity show less decline with age than those in which speed is a factor. Consequently the capacity for comprehension, reasoning, and judgment appears to be maintained at a relatively constant level as long as mental work and intellectual interests are continued.[17] Older individuals with active minds can in many situations compensate for the decline of quickness in comprehension by means of the greater knowledge that comes with age.[18]

With the gradual increase in age of the general population, our concepts of retirement for professional workers may require revision. Professors from universities requiring retirement at age 65 are often finding positions at other schools with no loss in academic prestige or status.

The underlying physiological bases of the sensory and mental changes which occur in older persons relate to an interference of normal metabolic processes within the cells of the brain and central nervous system.[19] This interference may operate through a reduced rate of transference of essential substances to the cells. Transference may be inadequate because of reduced supply, reduced circulatory delivery, or slower diffusion. Cortical tissue especially is extremely sensitive to a diminished supply of oxygen. There is a striking resemblance between certain of the psychological changes which occur with age and the same functions in younger subjects who have been deprived of oxygen. In one study in our laboratory, for instance, immediate memory was tested in various groups breathing air at ground level and simulated alti-

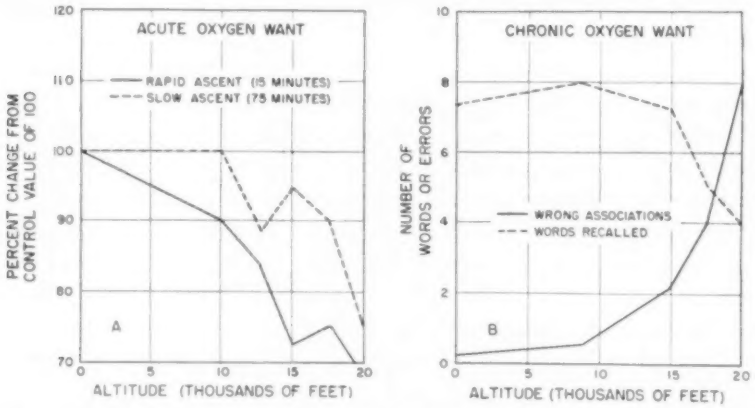


Figure 5. Effect of oxygen want (altitude) on immediate memory. The figure on the left indicates a significant decrement in objective tests for immediate memory at altitudes of about 10,000 feet or above during simulated flights. Impairment in words recalled and wrong associations was very marked above 15,000 feet in acclimated subjects on an Andean high-altitude expedition (right). (Reprinted by permission from *Human factors in air transportation,* by McFarland, R. A.[3] Copyright 1953. McGraw-Hill Book Company, Inc.)

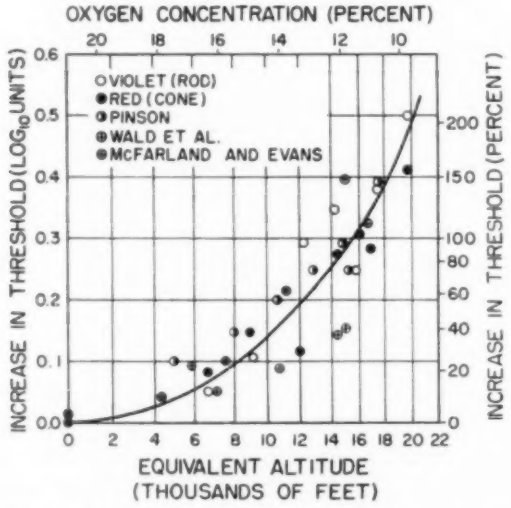


Figure 6. Effect of oxygen want (altitude) on light sensitivity. The curve shows the increase in threshold for light, or the decreased ability to see at night, in relation to altitude or oxygen pressure. Light sensitivity is impaired at altitudes as low as 5,000 or 6,000 feet. The percentage increase in light threshold at 15,000 feet is approximately 100 per cent: hence about twice as much light would be required to see a given stimulus under this condition. (Reprinted by permission from *Human factors in air transportation,* by McFarland, R. A.[3] Copyright 1953. McGraw-Hill Book Company, Inc.)

tudes. Throughout the course of these experiments, each subject was required to memorize several series of 10 pairs of unrelated words. The influence of age was revealed by the fact that, whereas the average college student could remember approximately 8 out of 10 words, their professors of about 55 to 60 years of age could recall on the average only 4 or 5. When the younger men were deprived of oxygen, however, their ability to remember was strikingly reduced, closely approximating the performance of their professors in normal air. Thus the older man's decline in memory may be attributable to the influence of lowered oxygen in the cerebral circulation and of impaired brain metabolism in cortical functions[2, 19] (Figure 5).

The findings of other experiments also show that losses occur in night vision after oxygen deprivation, similar to those occurring with age (Figure 6). A striking feature in normal subjects under low oxygen is a loss of insight into the quality of performance, parallel to that found in patients exhibiting abnormal social behavior and adjustment.

## Influence of Aging on Industrial Efficiency

The question now arises as to the extent these slight but definite functional decreases described above will influence the efficiency and safety of older workers. A definitive answer depends on comprehensive studies of productivity, labor turnover, accidents, and sickness rates. The prejudice against older workers was greatly reduced during and after the Second World War when they successfully replaced younger men. It has been amply demonstrated that older workers are safe and efficient if their changing abilities are continually matched with the operational requirements of specific jobs. In general, older workers are economical and successful for the following reasons: (a) They have fewer industrial accidents; (b) the labor turnover is smaller, thereby decreasing the expense of training new employees; (c) their output is usually equal to that of younger men, and they tend to cause less spoilage and general breakage; and (d) they tend to be more stable, loyal, and responsible. They are particularly valuable in situations involving little supervision.[20]

*Productivity:* Little information can be found for determining the role of age per se in industrial output. There are surprisingly few occupations in which a substantial number of workers are employed on work of equal difficulty, in which speed is governed by the worker

himself, and for which individual production records are maintained. In addition, a number of artifacts tend to obscure the true meaning of the data. In several extensive studies on production it was found that there is either only a slight positive relationship between industrial output and age, or none at all. On the whole, there is little convincing evidence that the production of older workers is less than that of younger ones.[20]

*Labor Turnover:* The training of new employees is, in many industries, frequently very expensive and time-consuming. The relation of age to frequency of labor turnover, or duration of employment, is therefore of practical importance. In general, the older worker remains on the job longer than does the younger one. An investigation of the records of four industrial concerns indicated a fairly steady and rapid increase in length of employment from 21 to 31 years of age, followed by a plateau and a further lengthening of service near the age of 50. In another study it was concluded that the greatest occupational mobility took place under 35 years of age; few shifts to new occupations occurred thereafter. From this point of view, the older workers are a distinct asset in terms of continuance on the job as compared with men in their 20's and 30's.[21]

*Accidents:* One of the most common reasons offered for discrimination against the older worker is that he is more of an accident risk than the younger worker. That this view is not justified has been demonstrated repeatedly in industry, automobile driving, and aviation. In terms of frequency rates, workers between 40 and 54 had rates only about 66 per cent as high as workers under 21, and 70 per cent as high as those in their 20's, in one study covering 26,000 employees in four plants.[22] The rate for workers of 60 years and older was lower than for those under 21, and about the same as for those between 21 and 29 years of age. A number of other studies agree with the general finding of a decline in accidents with age. In this respect, the only disadvantage of the older workers is that their disabilities last longer once they are injured; they require longer healing periods and more frequent dressings, especially those over 60 years of age.[2, 22, 23]

The frequency of automobile accidents is of interest in connection with the relationship between age and accident rates. In one study, the frequency of accidents by age was compared to the expected incidence based on the age distribution of drivers in the State of Connecti-

cut.[8] The 20-29 year age-group has a much larger accident-rate than would have been expected on the basis of the number of licensed drivers in this group. Individuals over 30 years of age, on the other hand, had fewer accidents in proportion to the expected number. The curve for persons over 60 tends to approach the curve for expected frequency. Similar findings have emerged from studies in other states, even when differences in miles driven at different ages are taken into account. Since the groups below 25 years consistently score higher on motor coordination and skill tests, the results of such studies have emphasized the need for training young drivers not only in driving habits but also in safe attitudes.[24] The higher accident-rate of youthful drivers has led certain automobile casualty companies to set rates partly on the basis of age.[25]

*Sickness and Absenteeism:* It is not possible to draw general conclusions about the frequency of illness among old people from statistics on absenteeism in industry, since only those in good health are usually able to retain their jobs. This was brought out in one study of industrial workers, which indicated a decline rather than an increase of sickness among older employees. It is usually true, however, that when older workers are ill, they tend to be absent from work for a greater number of days than younger workers. Thus greater attention should be paid to programs for maintaining a high degree of physical and mental fitness in the older worker, to reduce the incidence of sickness. Their useful lives can be prolonged by the early detection of latent illness and indoctrinating them concerning factors which influence their health.

When all of the above variables in regard to industrial efficiency and safety are balanced against each other in any given industrial situation, the value of each worker will vary with his productive abilities rather than with his chronological age. In most occupations, however, accumulated experience adds more effectiveness than does speed, or mere physical strength. Industry is well aware of the desirability of prolonging the useful lives of its older workers. In this way the social economy will be improved and the older person will be happier than if he is pensioned. The increase in the proportion of older people among the population makes the attainment of this goal increasingly necessary.

## The Influence of Aging on Personal and Social Adjustments

Age differences have been reported in regard to interests, attitudes,

emotions, and various types of social adjustment. It is not always clear, however, whether such differences represent changes due to age. With only a few exceptions the data in this area have been gathered from cross-sectional studies, comparing groups of different ages. A group now 20 years old may differ in various respects from a group 50 years, but this finding does not indicate what the current 20 year group will be like in 30 years. The differences found at present may not be due to age, but rather may result from differences in education, experience, social outlook, and other factors. As indicated previously, longitudinal studies are necessary to demonstrate age changes to the fullest extent.[4]

It is commonly believed that older persons have sounder judgment and take fewer chances than younger ones, and that the older individual is less favorably disposed to social change. Undoubtedly interests and attitudes undergo extensive changes with age, but no simple formula can be applied. The studies in this field do not indicate that older persons have fewer or wider interests, greater or less conformity to social demands, or inferior or superior capacities for adjustment. Not all younger men are delinquent or accident-repeaters, nor are all old men law-abiding and accident-free. Individual differences in interests, attitudes, and social behavior are pronounced in every phase of the life cycle. Individuals must be assessed in terms of their personal characteristics rather than in terms of their age, and longitudinal studies are more revealing than cross-sectional ones in studying human behavior.

The weakest link in understanding the psychological aspects of aging is in the field of emotional adjustment. Only a few methods of measurement have been developed, and we cannot appraise individuals on the basis of an "emotional quotient" comparable to the "intelligence quotient" of mental ability. According to the results of psychological tests, mental functions mature, or level off, at about 16 years of age. This appears unlikely in the field of emotion since maturity is normally reached much later. Possibly the premium placed on "speed" and the emphasis on "staying young" is a reflection of the emotional immaturity that is widespread in our society. Psychiatrists have developed certain techniques in interpreting and understanding emotional behavior and can make fairly reliable judgments about the adequacy of emotional adjustments. Successful adaptation to the problems of later life is undoubtedly determined by earlier emotional influences. There is great need for controlled studies in this field.

It has been shown in various psychological studies that the present dissatisfaction of many older people stems largely from anxieties about economic insecurity, the chronic diseases of old age, limitations of interests, and feelings of rejection by the social environment. Psychologists can aid greatly in making sound recommendations about the maintenance of a variety of interests, acceptance of change and participation in community life. Certainly physicians can minimize the anxiety over the so-called chronic diseases of old age. Even at the age of 75-80 years, only about 10 per cent of the population is actually disabled or unable to care for themselves. Since physicians are more apt to see those who are actually ill, it should be reiterated that age and disease are not synonymous. Obviously there is a greater possibility of illness with increasing age, but abilities rather than disabilities should be stressed. Special attention should be given to the maintenance of health.

## Summary and Conclusions

The process of aging follows no clearly defined course of events by which it is possible to determine accurately the "age" of any individual. In everyday experience, one frequently speaks of a person as seeming older or younger than his chronological age, or of a person as being old in years but young in spirit. These comments do not imply that a man of 20 years cannot be distinguished from one of 40, or the man of 40 from one of 60 years. The findings indicate that aging is, to a great extent, an individual matter and that there are many facets to the aging process. Some of the most important observations brought out in this discussion may be summarized as follows:

1. In appraising the capabilities of older people, the important variable to consider is not chronological, but rather functional age, or the ability to perform required duties efficiently and safely. Chronological age alone is rarely a reliable index of a person's physical or mental development and adjustment.

2. In the light of contemporary research, Osler's remark that "a man is as old as his arteries" might be extended to include the sense organs and the mechanisms of mental and emotional adjustment. Eventually a battery of tests may be developed in which visual accommodation, auditory acuity, light sensitivity, and other measures will be used to estimate "functional" age.

3. The natural process of aging is of more significance for some

occupational groups than others by virtue of differences in the demands made upon individual abilities. A defect in vision or hearing may be important for one occupation but not for another. Slowing reaction times may lead to loss of confidence in a task requiring quick responses. Corrective aids for defective vision and hearing can often overcome minor changes, and compensation through training or experience is often greater than the deterioration due to the aging of functions. Each individual should be evaluated, therefore, in relation to the demands of the job, and the amount of compensation he has developed. Physicians and psychologists have an important function to perform in matching the abilities of workers to the requirements of their jobs throughout the life cycle.

4. This survey of the findings in the field of the psychology of aging has revealed only few studies of a longitudinal nature, where the same individuals have been followed over a period of years. Most studies have been of a cross-sectional nature, on different groups by decades. The latter type of investigation has given rise to certain "stereotypes" in regard to age, and has failed to reveal the wide range of individual differences. There is little evidence to justify arbitrary retirements at 65 since each person's occupational future should be judged on its own merits.

5. The trends in studies of mental ability have shown that there is a sharp rise in scores to a peak around 20 years of age, followed by a gradual decline. Such tests involve specific time limits, and older persons are often placed at a distinct disadvantage. Judgment, reasoning, and other complex psychological functions are more resistant to deterioration with age. In fact many investigations have shown that if older persons want to learn or must learn a new task, they have the ability to do so.

6. In an attempt to explain the psychophysical relationships which exist between age and certain reactions such as vision at low levels of illumination, immediate memory, and loss of insight, it was suggested that the basic cause relates to an interference of normal metabolic processes within individual nerve cells of the brain and retina. The transference of oxygen may be inadequate, because of reduced supply, reduced circulatory delivery, or slower diffusion.

7. It was shown that the prejudices against older workers in industry are being minimized because they tend to have fewer accidents,

smaller labor turnover, and satisfactory rates of production. Furthermore they tend to be more stable, loyal, and responsible.

8. The experimental findings on the social behavior and emotional adjustments of older persons are more limited and less reliable. These areas are of the greatest importance, however, in successful adaptation to age. Physicians and psychologists can do much to aid older people in their declining years by encouraging them to maintain a wide variety of interests, accept personal and social changes, and participate actively in community activities.

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# PREVENTIVE USE OF PSYCHOTHERAPY IN CHILDHOOD

*Transcription of a Panel Meeting on Therapeutics**

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MODERATOR LAWRENCE S. KUBIE: Ladies and gentlemen, a difficult and complex problem confronts us all this afternoon. We have so little time that I will skip the usual formalities. Indeed I am not even going to start with the customary joke.

Our four panelists are two pediatricians, Drs. Clement B. P. Cobb and Milton Levine, and two child psychiatrists, Drs. Marianne Kris and Marian C. Putnam. They will discuss a problem which is basic for future mental health; namely, how effective is immediate psychotherapy for the earliest manifestations of neurotic disturbances in infancy and childhood as a method of prophylaxis against the fully developed neuroses and psychoses of adult life?

We have become aware that neither in our culture nor in any other culture of which we have much knowledge, is childhood free from recurring transitory episodes of distress. These may last hours or days or weeks or months or years. They may start as simple emotional turmoil and evolve into neurotic patterns. Or the emotional distress may be hidden so quickly that the first sign of trouble is the explosion of neurotic symptoms. In either case the traditional method of handling these upsets is to say hopefully that the child will "outgrow it." The question we must ask ourselves is whether this is good enough. This issue brings up many concrete problems, the first of which I will turn over to the pediatricians. I turn to them first because you could rightfully argue that the child psychiatrists, because of the very nature of their work, see a weighted sample and not a random sample of youth, whereas the pediatricians see a truer cross-section of the childhood in our culture.

Therefore, I will ask first Dr. Levine, and then Dr. Cobb to discuss the incidence of fully developed neurotic disturbances in childhood. Are these in fact universal? Secondly, what is the incidence of masked neurotic disturbances in early childhood?

DR. MILTON I. LEVINE: Any pediatrician or, for that matter any physician who follows a fair number of children in the course of his practice, cannot help but be impressed by the great number of neurotic symptoms seen in the growing child. Some of these are of long duration and appear to be deep seated while others are transitory, lasting but a short time. These disturbances, as mentioned by Dr. Kubie, are seen in the lives of almost every child.

There are numerous varieties—too numerous to mention individually;

so for the sake of brevity I will speak of those most commonly seen during the various age-periods of childhood.

During the infancy and toddler age level we are frequently confronted with toilet resistance and chronic constipation both of which, in practically all cases, are emotional in origin. A great many of the sleeping problems as well as the feeding problems during this period of life are also of emotional etiology.

Then there are the children who pull out their hair and at times eat it—and some children who pull off the fuzz of blankets or woolen dolls and treat it in the same manner. Temper tantrums, rocking and head banging are also common.

And then, usually during the two to three year period, we observe a great many fetishes. Many children carry old blankets, rags, worn dolls or animals around with them—and are dependent on these objects. If such a child loses this "treasured object" be becomes frantic, distraught, and even depressed for long periods of time. Another type of fetish seen during this same period is the almost compulsive need to have everything in a specific and familiar spot before the child will fall asleep.

In the pre-school period we frequently see habit-vomiting, especially during the first weeks of attempted separation from the mother at nursery school. Stammering, stuttering and the various tics may make their appearance during this period, although they may appear first or continue on during the school age level and even during adolescence.

The neurotic symptoms caused by separation from parents are also most common during this age span. Vomiting, sleep resistance, frequent awakening, stammering, stuttering, tics, bedwetting are among the many neurotic symptoms which may appear following separation.

Fear of dogs, cats or other animals, fear of noises such as caused by shower-baths, vacuum cleaners and airplanes are common in the pre-school age.

One also observes children with excessive sadism at this age level—children who will hold kittens and puppies by their tails and throw them around—or will find great pleasure in stepping on or destroying small animals and insects.

It is also during the pre-school period that we observe so many of the neurotic signs which arise in the course of sibling rivalry and sibling jealousy when a new baby enters the family. Soiling, enuresis, inability

to talk properly or walk properly, after these have been normally established, are common occurrences.

During the school age certain neurotic symptoms are also frequently brought to the attention of the pediatrician. Excessive masturbation is one of these. To Dr. Kinsey's question "What is excessive masturbation?" one might reply that from the pediatric viewpoint masturbation practiced to the exclusion of most other normal interests and activities may be considered excessive. Such a degree of masturbatory activity is always due to emotional difficulty.

Finger sucking, night terrors, tension headaches and certain cases of asthma and abdominal pain are also of emotional etiology and are frequently found during this age period.

Occasionally one meets with fetishes and compulsions during this period. For example, one particular child had to place her chin in her food before she would take a bite of it.

Anxieties, which are always emotional in origin, are not uncommonly met with during the school level.

Pre-adolescents and adolescents also seem to have certain special emotional problems with their subsequent neuroses.

Anorexia nervosa, a condition in which a child literally attempts to starve himself to death rather than face growing up, is not too uncommon. This is most frequently found in girls.

Some other neuroses during this period are kleptomania, anxieties and, again, compulsions.

During adolescence we observe cases of panic where a child who may or may not be a good student in school suddenly goes into an "adolescent panic." He can't study, "where is life leading me?", "why live in such a world?", etc. The panic may be closely tied to the child's anxieties about his sex role or heterosexual relationships.

These are some of the most common neuroses observed during the development of children. I am sure that every physician who deals with children meets frequently with these conditions. I am sure he can add other pictures of neuroses to the list I have presented.

MODERATOR KUBIE: Out of this answer, I would like to emphasize one point; namely, that to an extraordinary degree the varied manifestations of the neurotic process can be transmuted, one into another. Thus a child who starts out with any one of the constellations of symptoms which Dr. Levine described may change remarkably and spontaneously.

These symptoms may disappear, sometimes rapidly, only to reappear in other forms either at once or after a latent period. Nothing at all may show for a while. Then suddenly an entirely new group of symptoms may crystallize. From this fact we are forced to conclude that these varied constellations must be manifestations of a single and continuing process of psychopathology. If this is true, then the temporary disappearance of symptoms cannot be accepted as a return to health.

Dr. Cobb, would you pick this up now?

DR. CLEMENT B. P. COBB: I would like to say, first, that I agree with Dr. Levine that neurotic episodes are found commonly by pediatricians and by all doctors who deal with the young age-group.

Before I discuss in a general way the more frequent of these traits and manifestations, I would like to give a definition of psychiatry. This may explain what I will say later when I consider the percentage of children in normal pediatric practice who could perhaps be benefited by psychotherapeutic interference.

Psychiatry may be defined as that branch of medicine which deals with the genesis, dynamics and manifestations of such disorders and undesirable functions of the personality as to disturb either the subjective state of the individual or his relations with other persons.

On the basis of this definition, I recently reviewed 100 consecutive unselected cases from my private practice; that is to say 100 families, containing 147 children, between the ages of 2 and 13. I tried to estimate roughly in how many of these 100 families there were one or more children who could profit to a greater or lesser degree by expert psychotherapy. My conclusions were of necessity subjective and somewhat arbitrary; but I feel that they were conservative. I attempted first to decide whether such disorders and undesirable functions of the personality existed as would disturb the subjective state of the individual or his relationship with other persons, not only at the moment but in the future, sufficiently to warrant the introduction of skilled psychotherapy. This, of course, is not the same as saying that psychotherapy in all these cases would be available, economically feasible, or acceptable to the parents, whether for themselves or for their children.

With these limitations, then, my conclusions were that at least 46 per cent of 100 families presented one or more mild or severe problems that seemed to me to require psychotherapy. In 41 of these 46 families,

one or both parents seemed to me to show definite indications that psychotherapy would be of value. In 13 of the 100 families, it was felt that a child was getting along satisfactorily, but that one or both of the parents clearly showed the existence of neurotic traits which, if they continued unchanged, might induce character disorders and psychoneurosis in the offspring, especially in those families with young children.

MODERATOR KUBIE: *Can I cut in with a question which I would like to ask both you and Dr. Levine to answer? You have been reviewing your experience in private practice. I know that we have no precise comparative statistics, but is it your general impression that there is a significant difference between private practice and out-patient clinic practice with respect to the incidence of neurotic difficulties in children?*

*While this question is concerned primarily with the influence of economic, cultural, educational, religious and national origins on the incidence of neurotic difficulties in childhood, let us also ask whether there is a difference between boys and girls?*

DR. COBB: My general impression is that probably neurotic manifestations were as common in clinic practice as in private practice; but that because of economic and social differences and background, their detailed qualities might vary somewhat. But, as far as the influence on the happiness of the individual, or on his relationships to others, they were as significant in clinic practice as in private practice.

MODERATOR KUBIE: *Dr. Levine, have you an opinion?*

DR. LEVINE: I believe we see more neurotic symptoms generally in private practice than in clinic practice. Generally speaking, I think the parents of the clinic patient follow their normal feelings and instincts a lot better and a lot more frequently than parents of private patients who have been reading a great many books on the psychology of parenthood and often are not able to think for themselves. A good many of them try to follow situations exactly as the book directs and therefore, look up the pages immediately to see how they should react in every situation.

I don't believe that there is much difference in frequency of neurotic symptoms between boys and girls. I might add also that the clinic practice is usually composed of children of larger families which, again, makes a considerable difference. In larger families it is unusual to have so much attention focussed on the one individual child as is so frequently

found in the smaller families.

MODERATOR KUBIE: *I do not quite understand. Do you mean that since less attention is focussed on the poorer child, that child does not develop neurosis—or merely that the neurosis is not recognized as such?*

DR. LEVINE: I mean that where there is one child in a family there is a great deal of attention, over-protectiveness and often anxiety focussed on that particular child. Where there are a great many children there is often a more relaxed approach. We all have heard mothers say: "If only my first child had been born second." As families develop and there are more children, there is less tendency to have anxieties over one child and less tendency to over-protectiveness.

MODERATOR KUBIE: *Certainly the flapjack technique would have certain advantages, i.e., to throw away the first half-dozen and do a good job on the second half-dozen. How do the psychiatrists feel about this?*

DR. MARIAN C. PUTNAM: I think I would say only that in the child guidance clinics there are certainly more boys than girls. I am not sure that that means that there are more neurotic boys than girls in our society, but that they are brought to clinics, at least twice as frequently. In psychotic young children, in all clinics that I know about, there are about three boys to one girl.

MODERATOR KUBIE: *What age groups do you have in mind?*

DR. PUTNAM: I am thinking of pre-school children. In saying that there are two or three boys to one girl in child guidance clinics, I mean of all ages.

DR. MARIANNE KRIS: May I say something about the impressions which I have gained in working in day care centers? I work in three day care centers, which may represent selected groups inasmuch as all mothers work or are sick. Many of the homes are broken up. The incidence of disturbed children is enormous, no matter how many children are in the family, most likely because of the disturbances in the parents or in their marital relationships. I would say that the number of children makes a great difference. I think this is a secondary feature; though I would agree with Dr. Levine that some parents are much more anxious with their first child than with later children. But this, again, would be more or less true for the children of parents in the lower economic group too. They, also, have a first child, with whom they frequently are more anxious than with any of their later children. I

also have had the opportunity to observe a different type of group. There the families were selected only on the basis of their wish to participate in a longitudinal study and the likelihood that they would stay for many years in New Haven. This study is carried out under the direction of Dr. Ernst Kris at the Child Study Center, Yale University Medical School, under the direction of Dr. Milton Senn. The staff of the Center saw the parents before the child was born, and while the mother was pregnant. The incidence of disturbance in the children of generally normal parents (at least what we would accept as the average parent), is large. The group is small, but the high incidence of disturbance is quite impressive.

MODERATOR KUBIE: May I, as Chairman, interrupt this discussion here; because we must not spend all of our time discussing statistical impressions about an issue of fact which could and should be subjected to precise statistical inquiry. Unfortunately no such study has ever been conducted adequately.

Nevertheless it may be useful to note that as a panel we constitute a fairly representative cross section of pediatricians and psychiatrists, and that we are *not* in complete agreement about either the incidence of the neurotic process in early childhood, nor about its distribution among different economic or cultural levels. There is a better approximation to unanimity among us that the neurotic process is so widespread in our culture that it seems to constitute an integral part of our developmental process. Consequently we agree that the influence of early treatment must be subjected to a more careful appraisal than has ever been given to it. I think that on this we are all in full agreement.

I am glad that Dr. Kris made her point so explicitly about the enormously high incidence of neurosis in childhood: because this turns our attention away from the melodramatic and exceptional experiences of childhood to all of the humdrum experiences of a child's daily life,—how he falls asleep and wakes up, the exercise of the daily functions of the body, the universal experiences of daily rivalry in the nursery, the overpowering emotional stresses which result from being small in a grown-up world. These banal daily events are the soil out of which the neurotic process grows,—accentuated and exaggerated and altered and modified and molded though it may be by more individual and exceptional experiences. These special stresses exercise their influence around a core of experiences which are common to all of childhood.

About this we of the panel seem to be in considerable measure of agreement.

Now comes the critical point: what are we to do about this? Is there anything we *can* do about it? Here I am going to turn first to our psychiatrists, and ask their opinions. *First, what is the outcome of the traditional method, the brushoff technique; i.e., letting the child "outgrow" it? Dr. Cobb and Dr. Levine have described widespread transitory and lasting neurotic disturbances in childhood. What is the ultimate influence on these of the traditional "laissez-faire" policy?*

DR. KRIS: This is a difficult question. Frequently we must make a decision at a time when we really do not have—and actually cannot yet have—thorough knowledge of all causative factors. Parents bring a child with symptoms and ask: "Should we do something about it now?" Sometimes at early ages we may think that some of these symptoms will disappear spontaneously. I mean, in the sense that the growth process and the strengthening of the personality may be able to cope with the problems of the child without any further signs of pathology.

But frequently—and I am afraid that this is more often the case—we will find that advice of a superficial nature is given for children, for instance for some with sleeping disturbance: "Well, just put on a light, and that is all." The child may actually fall asleep more readily, but at some later time we may observe the progress of this child and find that while, through the mechanical help, the sleeping disturbance may not be apparent, other disturbances appropriate to the age of the child may have become manifest. At that time we find that we definitely do have to step in with real therapy.

The question arises whether we could perhaps have obtained better results if we had intervened earlier. That is, if we intervene during the years when unhappiness begins to invade the family, before the one child's disturbance begins to affect the siblings, and before the parents in their turn react apprehensively to the whole situation, could we not have rescued a whole family? Therefore I think it is important to know what are *normal* incidents. Many manifestations may be disturbing for the parents, but nevertheless they are normal incidents in the development of the child.

I would like to emphasize that not every sleeping disturbance is immediately to be taken as a neurotic symptom. We do know that at a certain age level, between three and six, for instance, every child has

a tendency to disturb the parents in their bedroom. He may want to separate the parents. This is an interruption of the child's sleep as well as that of the parents. But this is a normal incident and, if handled correctly, it need not lead to any neurotic disturbance.

My special stress would focus on the attempt to prevent unnecessary wrong handling of such normal incidents. Careful observation of these incidents should make it possible to pick up at an early time those that do not fall in this category of the normal. Rather than be left to be outgrown, they could be taken care of in various right ways, either through the psychiatrist talking to the parent or directly with the child. These are variations depending on the type and degree of the disturbance. Early diagnosis is important.

MODERATOR KUBIE: *Dr. Putnam, do you want to pick up this question?*

DR. PUTNAM: Perhaps it is going ahead of our discussion to say that this certainly points to the need for psychiatric consultation centers, where a mother can go without the expectation of inevitably being taken in to treatment, either herself or the child, but where she can discuss something that worries her about the child's behavior. Here the attempt can be made to decide empirically, by giving some advice and by giving the mother an opportunity to talk over what she thinks is going on in the child, to decide whether this is something which can be taken care of in two or three or four understanding interviews, either with the family physician or with the psychiatrist, or whether it is something which should immediately come into treatment.

Such consultation centers hardly exist, I think; and certainly this is an important function of the child psychiatrist. Perhaps we could develop our well-baby clinics and nursery schools as screening centers much further than we do.

MODERATOR KUBIE: I think that our area of agreement grows. We seem to agree that the method which we have used in the past, i.e., of dismissing the child's transient emotional and neurotic disturbances, hoping that he will "outgrow" them, and waiting until they get a strangle-hold on the child before we pay serious attention to them, is fatal. We agree that if we are going to use psychiatric exploration and psychotherapy for preventive purposes, our efforts must be made much earlier. This seems at least to be the consensus of feeling among the pediatricians and child psychiatrists of your panel.

I would like therefore to ask our pediatricians how to integrate the roles of the pediatricians, of the general practitioner, and of the child psychiatrist in approaching this problem. And, if we were to broaden our thinking, I would ask them to consider also the role of special schools and social agencies.

*In short, if there is agreement on fact and on policy, how then are we to implement that policy by integrating the pediatricians, the general practitioner, the family physician, the child psychiatrist, and the various school and social agencies in the introduction of diagnostic and psychotherapeutic processes early in the development of the neurotic process, for preventive and prophylactic purposes? Dr. Cobb!*

DR. COBB: I agree fully with what the psychiatrists have just said. But about the possible contributions of the pediatrician and of the general practitioner to the avoidance of some of the neurotic disturbances which we have mentioned, I would like to hear the experts, Dr. Kris and Dr. Putnam, and their practical suggestions; e.g., how would they avoid feeding difficulties, or handle toilet training? At what age should it be done? How educate the parents as to their attitude in the matter? How treat the child's worries over sex differences? How to handle sibling rivalry? How to encourage the development of a child by encouraging the process by which he grows up to identify with the parent of the same sex at the proper age? How to avert the traumatic effects of certain unnecessary operations at certain ages, such as the operation of circumcision, for example? I have seen that performed on a child of one year with disastrous effects on the child's nervous reactions.

Those questions cover a few highlights on problems about which the experts could help with their advice to the pediatrician and to the general practitioner.

DR. LEVINE: I, also, agree fully with Dr. Kris and Dr. Putnam on their approach to this subject. Certainly the old "brush-off" technique, and the reassurance that the child will outgrow these particular neuroses has no place in modern pediatrics. It is my hope, however, that the coming pediatricians, now still in medical schools, and the present-day pediatricians as well, will gain an adequate background; so that they themselves will be able to handle certain of these problems and will be able to do the screening process themselves as to which child needs more specialized psychotherapy, and which child can be handled by the

pediatrician himself. He has to remember, of course, that there are no definite rules; that every child is different, the home environment is different, the background is different. The pediatrician must take sufficient time to get a good history. He has to have a good understanding of the norms of child development, so that he is able to interpret the deviations. He must have some understanding of the depth of the neurosis, and he must know whether he himself as an individual with his particular background is capable of handling it.

It seems to me that a good many of the neuroses that Dr. Cobb just mentioned can be handled successfully by the aware pediatrician; and there are at the present time means by which a pediatrician may get a certain amount of the background necessary to handle the more superficial problems which do not require the attention of a trained psychiatrist.

MODERATOR KUBIE: I would like to pose a question here. Dr. Putnam and Dr. Kris have spoken of the importance of early psychiatric consultation for diagnostic appraisal. They also speak, and rightly, of the importance of early intervention by the pediatrician who is psychologically and psychiatrically aware. Now, if we consider the integration of the two, the practical question that arises is who should decide, and how, whether a child's upset is superficial or deep, whether a seemingly superficial symptom covers a more deep-seated neurotic process. Is the decision to be made on the basis of psychiatric examination and psychological testing, or should it be made by trial and error, that is to say by seeing how far the pediatrician can get with superficial therapy?

I would like you to discuss this, if you will, and then we will pass it along to the others.

DR. LEVINE: If we, as pediatricians, are able to develop a broad enough background, in certain of these common neurotic aspects of child development, we will be able to advise a parent satisfactorily. Many of us are able to follow children very closely in private practice. That is one distinct difference between private practice and clinic practice. In private practice, we have the opportunity to go into the home; we see the home and living conditions, and we are able at times to watch these neuroses develop. We are in on the ground floor. The psychiatrists, on the other hand, have to delve into the past to get out of the child what has happened. If we are aware, as physicians to children, we can at times observe what is happening and alter the course

or even stop an oncoming neurosis.

I feel strongly that a trained pediatrician, with psychological and psychiatric awareness, can himself attempt to treat a good many of the minor psychological situations that occur, situations that arise out of sibling rivalry, for instance; although I agree entirely with you, Dr. Kubie, that some of these situations may look superficial, yet may be much deeper than any of us imagine at first sight.

I would not exactly call it a trial-and-error procedure. I would say that we ought to try to see if we succeed, and if we feel that we are capable of doing so. If we find that we are unsuccessful, that the child is not improving at the rate we had expected, then I think it is time for us to advise a psychiatric consultation.

DR. KRIS: It seems to me that the pediatrician is in a strategic position to prevent the development of many pathological phenomena, whether in private practice or in well-baby clinics, or in hospitals. This is the area where the pediatrician is the person to do the job. The mothers come to him early, usually right after the baby's birth, so that he follows the development from the beginning on. If well trained in psychiatry in medical school (and I think a thorough knowledge of child development should be stressed in the educational background of every pediatrician), he can always prepare the parents for what is to come, what difficulties to expect. And here I would like to pick up the phrase Dr. Levine uses, "sibling rivalry." I want to emphasize that this is a normal phenomenon, not a neurosis. It can also be the symptom of a neurosis. But, we expect sibling rivalry in every case, and we would be astonished if parents tell us that they have never noticed any signs of it. That is the moment when I become suspicious that something is wrong.

As long as these incidents are neither too intense or long-lasting, nor take sharp turns, the pediatrician can help the parents deal with the phenomena that Dr. Cobb has mentioned, like feeding, sleeping difficulties, toilet training, etc., and thereby prevent wrong attitudes.

I should like to mention another approach to help parents. The Child Study Association conducts parent groups, where parents can discuss their problems with a leader especially trained in child development.

MODERATOR KUBIE: The issue here is most difficult, not only in relation to pediatric practice and the application of psychiatry and

psychotherapy to childhood, but in the current effort to integrate psychiatric methods and psychotherapy into medicine and surgery in general. The question is how much the general practitioner, the internist, the surgeon, as well as the pediatrician can and should do himself and at what point he should bring in psychiatric evaluation, at what point he should bring in technical psychotherapy. I have no illusion that we are going to answer this question here this afternoon. It is perplexing all medical educators today, both because it is difficult and because the answer covers important implications for medical education in general.

The simplest form of dilemma is the one which I proposed to Dr. Levine. Should the pediatrician, when the patient is a child, or the general practitioner for an adult, *always* do all that he can first? How long should he continue his efforts? How long will it be before the neurotic process jells and becomes "chronic" and more difficult to deal with? How early, then, should he bring in technical help?

In all fields of medicine there are certain individuals who have, in addition to their general or specialty training, a high degree of native psychological aptitude. These exceptions cannot however be taken as the standard for all. We have to consider this question in terms of the more average practitioner, the more average pediatrician. How far shall he go in his effort to evaluate and to treat neurotic illness? At what point does he bring in the specialist? This does not cover the whole problem to be settled about the integration of psychiatry into pediatric practice, but it is one of the important initial problems on policy in the relationship between specialists.

*Dr. Cobb, how, in your opinion, should we integrate the general practitioner, the pediatrician, and the psychiatrist?*

DR. COBB: Well, it seems reasonable to suggest that the well-oriented pediatrician (and we hope that the pediatrician of 20 years from now will receive a better psychological background from his medical school education than do the pediatricians of our own day), should follow such a case, particularly where he knows the family well, doing what he can particularly with the parents, reassuring when indicated, directing when possible. Then, if he finds that the condition of the patient is becoming progressively more unsatisfactory to the parents or to the school group, or that the patient is becoming progressively more unhappy, then it would seem that the logical thing to do would be to suggest to the parents that a psychiatric evaluation is in order. He may not neces-

sarily use that phrase, but something similar to it. He will find that most of his parents are quite cooperative. He can explain that an intelligence test is often helpful, and that there is something called a Rorschach test which, in the hands of an expert evaluator, can also be helpful, and that the interview with an expert in a case such as this particular child may enable the family to make up their own minds as to whether intensive psychotherapy is indicated or not.

MODERATOR KUBIE: This problem is crucial. We are in agreement, apparently, as to the types of problems which arise in childhood. Moreover we seem to be in agreement that some degree and kind of early intervention is necessary. *What we are still perplexed about is by whom the intervention should be initiated, how early, and what form it should take. I will toss this back again to Dr. Levine.*

DR. LEVINE: Well, I believe, Dr. Kubie, that there are certain definite situations that a pediatrician—I should say an aware pediatrician—can handle; and I also feel that there are certain other situations that a pediatrician, even with some psychiatric background, would find very difficult to handle and should almost immediately turn over to a psychiatrist. The situations that can be handled would include emotional constipation, many of the sleep problems, tension headaches and tension abdominal pain, many of the separation anxieties, temper tantrums, many of the neuroses born of sibling rivalry, like soiling and wetting, fear of water, noises and shadows, and so forth. Those can often be handled successfully by a pediatrician with the proper background.

On the other hand, there are certain situations (and I speak from experience), which it is almost impossible for a pediatrician to treat adequately. Enuresis in the school age child is of this nature and is difficult to eradicate unless one wants to resort to the apparatus that rings a bell, waking the child the minute the child wets. Of course this doesn't remove the underlying cause of the chronic enuresis but it does remove an embarrassing and upsetting condition. Some of the severe habit spasms, and stammering and stuttering, are usually of emotional origin. And there is the anxiety neurosis, where a child is fearful of everything without any known reason. The child may say of a stethoscope: "I know it can't hurt me, but I'm afraid of it." Anxiety neuroses are usually too deep for a pediatrician to handle successfully. Abnormal aggressive behavior also occurs during this age period. Adolescent panic, which I mentioned before, kleptomania and the compul-

sion neuroses—those are but a few situations that I think are beyond the capabilities of the average pediatrician and deserve psychiatric treatment.

DR. PUTNAM: I would like to add simply that it is difficult to tell from the symptom whether this is a real neurosis or a manifestation of some transient conflict. Vomiting may have occurred daily for weeks or months and still be easily remedied with a few consultation hours. On the other hand, it may be the symptom of a profound neurosis. Therefore early and periodically repeated psychiatric consultation may be necessary before either the pediatrician or the psychiatrist himself can decide how much technical therapeutic intervention will be required even for a seemingly minor symptom.

DR. KRIS: I agree with Dr. Putnam. We cannot go solely according to a symptom, though we would perhaps consider one symptom more dangerous than another.

With stammering I would, for instance, be more inclined not to wait a year, because once stammering is fully established it is one of the hardest symptoms to remove. If we get at it fairly early, we frequently can discover the original circumstances which gave rise to the symptom. We can find out much more of what is going on at the very time when the disturbance begins, and help the child in various ways, as well as prevent the family from developing traumatizing attitudes. In direct therapy with the child we can find out some of the fantasies that are causing the disturbance. In any case, we have to try to find what the symptom means in the special situation, and only on the basis of this knowledge can we form an opinion as to whether it is apt to be a major or minor incident. I would be inclined to take a more serious view if a symptom has persisted for more than a year. By that time it may form a more integral part of the personality structure. That is, it is no longer merely an isolated symptom but a sign of the establishing of a more complex neurosis. Nevertheless, this does not mean that I would object to symptomatic treatment at all times. If a symptom burdens and hampers the development of the child, every attempt should be made to free the child from the further traumatic effect of the symptom, even though such an approach will not remove the underlying disturbance.

DR. COBB: I would like to ask Dr. Kris if she would agree that a tic in a six or seven year old child is as positive an indication for therapy as stammering? It would be my impression that it would be.

DR. KRIS: I agree fully with that.

MODERATOR KUBIE: We are challenged here by several difficult problems. One is the issue of how to integrate different agencies and different specialties in the introduction of early therapy. The other, and perhaps the deeper one, is one of the oldest problems in all of medicine, not peculiar to psychiatry or pediatrics alone, i.e., when to treat a symptom and when to treat a disease process. As Dr. Kris has said, certain symptoms are so burdensome that you have to bring to them whatever relief one can; just as, with few exceptions, we give relief for pain, even when we know that we are not curing an underlying disease. Sometimes this carries the danger of obscuring a process of disease by alleviating the symptom.

The same thing is true in dealing with neurotic problems, and especially with the ubiquitous masked neurotic difficulties of early childhood. This requires careful judgment, i.e., when to allow a child, or a family, to suffer from a child's neurotic symptoms, when to bring them to treatment, or when to give them palliative relief, because the symptomatic difficulties are putting an overwhelming burden on the child's development. Certainly we would agree that there are no fixed or general rules for this. Yet we must raise the question, because we have been governed unwittingly by a general tendency always to cure (i.e., mask?) the symptom at any cost. Sometimes the cost is that we dissipate the symptom and turn our backs on the underlying psychopathological process with unwarranted satisfaction, as for instance over the fact that we have helped a child to stop having nightmares. Sometimes in the long run that child and his family pay a heavy price for this, if we fail at the same time to find out *why* the nightmares occurred and fail to eliminate their underlying cause.

*A number of questions have been passed up to me, some of which should be discussed. I have grouped them together under various headings. One group brings up the question of the interrelation of organic and psychological patterns. Some in the audience have asked: what is the role of constitution? One caustic challenge comments that "as usual, nothing is said about personality and constitutional differences." It is true that nothing has been said about this so far. I will leave it to the members of the panel to say why, and to deal with this question. Who would like to answer this question, i.e., to discuss the influence of possible constitutional factors on our policy with respect to early treatment?*

DR. LEVINE: I think it might be said that every pediatrician realizes that, almost at birth, there are different types of babies constitutionally. We recognize certain children as hypertonic children. These are children who are more keyed up. They are active babies who hold their heads up on their necks the first day they are born. They push themselves up on their arms when they are a few days old. They are more likely to develop colic. They are more likely to respond quickly to noises around the house. They jump quickly.

Then, you have the other type of child who is calm and complacent. I think the children that are hypertonic may present greater problems later on because of certain tensions that exist. They may react in a way that creates more anxieties in the parents than the calm, complacent child. Generally speaking, I think that most of the neuroses that occur in childhood, however, are based not upon the constitution, unless it starts at that early stage, but are based upon experiences and family situations and the environment of the child as he goes through this period of development.

MODERATOR KUBIE: Thank you, Dr. Levine.

*Is there anything that either of the psychiatrists would like to say about the question of constitution?*

DR. KRIS: I may perhaps refer again to the longitudinal study at Yale I mentioned before, that has this problem very much in mind, namely, to relate constitution and development and environmental influences. Interesting facts have come out: the importance of constitution in determining many vicissitudes of the future development, and particularly the reaction of the parent to the manifestations of the specific constitution of the child.

MODERATOR KUBIE: *The next group of questions deals with problems of organization; i.e., the ways in which schools, social agencies, pediatricians, psychologists, psychiatric social workers and psychiatrists can be brought to a focus on these problems.*

*One question asks how often the pediatrician is brought into "the famous psychiatric team," which usually consists of the psychiatrist, social worker and clinical psychologist, with no mention of the pediatrician. The mere asking of that question is a challenge to us.*

*Another question is concerned with pre-payment plans for early psychotherapy, i.e., whether there could be any way of organizing groups of young couples, even before they have children, into pre-payment*

*groups, which would make it possible for their babies and children to receive periodic psychiatric checkups and treatment as needed, and for the young parents to participate in group seminars and to receive group training. In modified forms that has been tried all around the country, through the early counselling for young parents, which the Child Study Association of America has provided for many years.*

*Among these questions about organizations one finds the comment that much of the responsibility of the pediatrician in the first year of an infant's life really consists of psychiatric education for the parents. You will realize that most of these are challenges rather than questions. It is worth while to bring them into focus here and to consider them together.*

*The next group of questions deals with various difficult problems with which members of the audience have had to deal. I will run through them, and then ask each member of the panel to discuss those particular topics which are of special interest to him.*

1. *How does one deal with asthma in adolescence, and what is the influence of early psychotherapy on asthma?*

2. *How does one treat nightmares or general nocturnal restlessness; and when should nightmares be taken as an indication of something seriously amiss in a child's development?*

3. *What about the withdrawn child? How can one distinguish between the benign shyness which appears at certain stages in the development of every child and a more serious pathological withdrawal?*

4. *How can one overcome parental pride and parental resistance in bringing either the parents or the child to accept psychotherapy?*

5. *What is the significance of girlish behavior in a three and a half year old boy who likes to put on his mother's clothes and to play with dolls?*

6. *Then, we are back to the problem of enuresis, which has already been discussed.*

*I will ask our panel to pick up any one of these questions. All are of great interest.*

DR. KRIS: I will discuss the girlish behavior in the three-and-a-half year old boy. Naturally, I could not say what its significance in this specific child is, without knowing many more details of his history.

I might indicate one possibility that may cause this development. A mother, who really did not want a boy but hoped for a girl, would

in many ways express this wish, for instance, by dressing the boy daintily and letting his hair grow long. She will perhaps give the boy only dolls to play with, and encourage this play more than what we call "the boyish games." She might not allow him to go out and play with other boys. That mother's preformed idea of the child certainly would have a great influence on the child's attitudes and conception of himself.

We know that every boy goes through a period in which he may have some fears about his maleness. But, if it goes so far that he gives up his male identification and only wants to be a girl, then we must assume that pathology of a more serious nature has established itself.

To prevent misunderstanding, I am not talking of constitutionally determined cases but rather of psychologically motivated ones.

MODERATOR KUBIE: *Who would like to take up the next question?*

DR. PUTNAM: The question about the withdrawn child as differentiated from shyness. We have seen many so-called withdrawn children in our clinic, and I think that one can differentiate them, and I always wish it had been done much earlier. We almost never see the withdrawn or psychotic child until over a year after the process has become clearly manifest. It is one of the things which may occur suddenly following a separation from the parents. One can sometimes look back, then, and see indications that this child had already been in trouble.

But, where it occurs suddenly, and there is a change in disposition, and the child no longer wants to look at people, and loses such achievements as toilet training, which is dependent on a desire to be like older people, and when the child becomes extremely solitary, and also narrows his play down to some stereotyped pattern of play, such as twirling something, or something of that sort, and his general development does not go ahead: these are serious early signs of danger.

I think that is the principal difference between the withdrawn child and the shy child. The shy child will still continue, usually, to learn to make friends, to develop with those with whom he is not so shy, whereas the withdrawn child shows to a high degree a slow development and, even, regression.

MODERATOR KUBIE: *We have less than 15 minutes more. We cannot cover all of the questions that have been raised. I will ask Dr. Cobb and Dr. Levine to pick up whichever of these questions happens to interest them most; and then I will say a few words to close our meeting.*

DR. COBB: I could discuss briefly the subject of asthma in adolescents.

It would be difficult to discuss any specific case conclusively without a history. But, it seems to me that in asthma in an adolescent, the first thing to do, of course, is to obtain a careful history. We know that the causes of asthma in an adolescent are like the causes of asthma in children of younger ages and, also, in individuals who are older than adolescents.

Sometimes asthma is brought on by respiratory infection. Sometimes it is brought on by inhalants, sometimes by foods (although this is less common). What would be most unusual is for asthma to occur in an adolescent for the first time: whether as a consequence of emotional causes, physical causes (such as exposure to cold air), or chemical irritants, and so forth.

If the asthmatic attacks occur in association with hay fever, which is appearing in the adolescent for the first time, one would think strongly of the possibility of pollen asthma. According to the history, therefore, the child would probably require skin testing for the likely inhalants or the pollen that might have precipitated an attack. Perhaps stripping the room would be in order if the child was found to be sensitive to any inhalants at all.

If the attacks seemed to be chiefly on an emotional basis, and if the child seemed disturbed, then unless the family doctor or the pediatrician could establish considerable rapport with the patient, and unless they had both knowledge and skill in superficial therapy at least, they should refer such a patient to someone with special training in psychiatry.

MODERATOR KUBIE: I will add one word to what Dr. Cobb has said. From previous discussions I know that he had it in mind, too, but it is important to make it clear that this is not an either/or business. The child that suffers from asthma suffers from one of the most traumatizing experiences to which a human being can be subjected, i.e., the inability to breathe. The earlier in life that this happens for the first time, the more devastating are the consequences. This makes it difficult to be sure to what extent the personality, which has sometimes been described as being the asthmatic personality, is a consequence of the asthma, or to what extent it is productive of the asthma, and to what extent circular cause and effect relationships are operative. In addition, the asthmatic child develops a sense of the helplessness of the adult world on which he has always depended. This in turn has an impact on his entire relationship to the adult world.

*It is impossible therefore for a child to suffer from asthma without gathering around that asthmatic condition devastating emotional sequelae, no matter how chemical its origin. Therefore many physicians contend that a unilateral or one-sided attack on the problem of asthma, whether from the organic-chemical, or from the psychological side, is doomed to fail. Would you agree, Dr. Cobb, that it has to be a double-barreled attack?*

DR. COBB: I agree entirely. If I might briefly cite one instance, I would like to mention a four year old child with an allergic eczema and chronic asthma, who was a wretched, unhappy, sleepless, disagreeable little child, greatly under weight. He was studied at some length with skin tests; and he continued to have asthma until someone picked up the fact that in one of the tests his mother's face powder had proved positive. Nothing had ever been done about it. The mother was then put on non-allergic cosmetics and miraculously, the child's allergic eczema and asthma disappeared and the child put on weight. Yet for several months great effort had been made to put this child into psychiatric care. When he was brought to the allergy clinic at the hospital, a month after the exposure to the powder had been stopped, the pediatrician who saw him did not recognize him; he had gained so much weight and his whole aspect was entirely different.

The mother said that there was no use in continuing to seek psychiatric care; that it had become unnecessary. In no other case, however, have I ever seen such a dramatic instance of the elimination of a physical disability resulting in a completely changed personality, as in this particular small child.

DR. LEVINE: I will spend a brief moment on the subject of overcoming parental resistance to getting a child in to psychiatric treatment. As we all know there are many people who resist any suggestion concerning sending the child for psychiatric care or even study.

There are a number of approaches to this problem. Of course, the best method is to know your patient and his parents well and to give the parents a feeling that you understand their problems and are interested in the future happiness of their child.

I think using the term "guidance expert" first, rather than using the term "psychiatrist" is often advisable, since the word "psychiatrist" bothers a great many people. Then, there is another way which usually works well, i.e., where the physician can "pass the buck," that is by

referring a patient to an organization, like the Child Study Association. People will usually go to such an organization without any question, and are more likely to accept the suggestions made there by the guidance experts.

DR. KRIS: I shall try to answer the question on nightmares. We frequently hear of children having nightmares. This need not indicate a severe neurosis. However, we would consider the nightmare as a more serious problem if it occurs in a long series. Frequently then if we look closer we find that the nightmare is not an isolated symptom. There are other smaller or larger deviations in other areas too. We may use enuresis as a parallel example. Often parents bring a child for treatment only because they are disturbed by the child's bed wetting. Invariably, when we look further into the details of the case, we may find, for example, that the child is a sloppy child, more than average for the age group; that there was some stealing, temper tantrums, etc.

The same is true of nightmares. We frequently find that the child suffers from anxiety not only at night in the form of nightmares, but also from many fears in daytime. He may be over-shy, or he may fear physical injury and therefore, for example, be unable to play football. The examples can be multiplied. The essential point, however, is that we must look not only at the symptom itself but at its intensity and the surrounding circumstances in which it occurs.

MODERATOR KUBIE: We have reached the hour at which we are forced to close our meeting. I want to thank the members of the panel and the audience for your patience, your interest, and your helpful, useful and provocative questions.

I would like to add one point as an elaboration of what Dr. Kris has just said so as to sharpen the central issue that we have in mind. At the Neurological Institute this morning we saw a ten year old child, who could have furnished the text for our entire meeting this afternoon. Her complaints were nightmares, from which she had suffered for five years. They were more than nightmares, because they evolved into experiences of frantic terror, with vivid hallucinatory dream-like experiences. These were always about snakes.

The child, at the onset of this upset at five, had tonsillitis and ran a temperature of 105°. This became a critical event in the child's life; because during a brief delirious episode, she had vivid and disturbing hallucinatory experiences, from which she would awaken both fright-

ened and confused. Delirium is not a complete sleep. Nor is it completely awake. Every child struggles with difficulty to achieve the ability to distinguish between reality and dream. She had never fully established that differentiation, before the delirious episode occurred to set her back.

On top of this a couple of other mishaps occurred. Her stay in the hospital, which was for only a day or so, meant her first separation from her mother, who was pregnant. A month later her little sister was born. Then, to cap it all, a few days later she encountered a little boy who chased her while holding out a dead snake. It was then that her neurosis took definite shape.

Here in a nutshell is the story of the development of one child; who for five years since that time has spent her every waking hour holding in check the free play of her imagination, free fantasy and free thinking of which she should have been capable. Her entire development has been blocked. In an adult we would have called those years, five years of living in a severely retarded depression, if not something worse. But a child who goes through a few months or a year of this loses that much time of fun and play and schooling and companionship. The secondary consequences of these few pathogenic moments can thus be enormous. Could immediate attention to these consequences have prevented or minimized their cumulative destructive impact?

This is why we feel that we must learn to pay more and earlier attention to the many minute events of childhood, which seem to be so banal, so deceptively innocuous and unimportant merely because they are part of everyday life.

# ROBERT ABBE: PIONEER IN NEUROSURGERY*

HERBERT PARSONS

ALTHOUGH this paper is intended to present an account of Dr. Robert Abbe as a pioneer in neurosurgery, it would not be correct to think of him as a neurosurgeon in the modern concept of specialization any more than to classify him as a plastic surgeon or radiotherapist. He was, in fact, primarily a general surgeon with interests extending into many fields of medicine and surgery. It would therefore seem permissible, in order to give a more accurate picture of his versatile nature, to include in this discussion something more about his contributions to general surgery in addition to those dealing directly with neurosurgical subjects. There are also some things about his work at St. Luke's Hospital and the Abbe museum at Bar Harbor which may be of interest.

Following his graduation from the College of Physicians and Surgeons in the class of 1874 and his internship at St. Luke's Hospital from 1874 to 1876, Dr. Abbe's surgical training was completed under the preceptorship of Dr. James L. Little. St. Luke's Hospital at that time was situated at Fifth Avenue and 54th Street on the site now occupied by the University Club. Dr. Abbe was appointed to the attending staff. He also became attending surgeon to the out-patient department of the New York Hospital, then located on 16th Street. He soon became recognized as one of the leading young surgeons in the city.

Among his medical friends were several who were interested in neurology, in particular Dr. Charles Dana, Dr. Edward Seguin and later Dr. Pearce Bailey. Dr. Dana became professor of neurology at Cornell and Dr. Seguin professor of nervous and mental diseases at the College of Physicians and Surgeons. Dr. Bailey was one of the founders of the Neurological Institute in New York and for a number of years was the neurological consultant at St. Luke's Hospital.

Stimulated by the enthusiasm of these men Dr. Abbe became interested in the surgery of the nervous system, notably of the spine

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and cord. This period of the early development of neurosurgery in New York was well described by Dr. Byron Stookey in his Elsberg Lecture in 1951.[1]

Dr. Abbe has been credited with the first removal of an extradural cord tumor in this country. There were two patients reported by him in which such an operation was done. It seems probable that in the first of these cases the mass which was thought to be an extradural tumor was in reality tuberculous but this is not certain. The operation was done on May 26, 1888 and the case was reported at a meeting of the New York State Medical Society early the next year.[2-4] The patient was a 22 year old man who was admitted to St. Luke's Hospital because of pain in his back of three months' duration. Gradually, while in the hospital, he developed a right paraspinal mass in the lower thoracic region, and a progressive loss of sensation and motor power in the legs with involuntary muscular twitching and incontinence of urine and feces. At operation the laminae of the eighth, ninth and tenth dorsal vertebrae were removed and a "mass of tissue and dessicated pus" which compressed the cord against the anterior wall of the spinal canal was removed. Eight days after operation, sensation began to return, his pain disappeared, and by the "fourth week he began to move his left leg and the toes of his right." He continued to improve over the ensuing months so that eight months later he walked "well and without support," was "stout and hearty and since operation absolutely without fever or evidence of tuberculosis. The tumor tissue was examined for bacilli but nothing but cellular tumor elements and pus found." Two years later this further comment was made about this patient:[5] "He resumed work and remained in perfect health for two years walking as well as ever and without fatigue. Recently, after confinement of the winter, he has had an abscess form in the cicatrix which had been so long healed and I have had to curette a sinus remaining from it." This had a "distinctly tubercular appearance."

Dr. Abbe[5] operated on another patient with an extradural cord tumor on April 16, 1890. This second patient had developed a complete paraplegia eight months previously. Although the diagnosis of cord compression had been accurately made by Dr. Seguin and operation advised, there had been considerable delay in getting around to it. The patient's condition was not good; he had been running a fever, and had albumin and casts in his urine. At operation the arches of the eighth,

ninth, and tenth dorsal vertebrae were removed and a "firm, dark growth was found to fill the vertebral canal, compressing the cord to the left side and flattening it somewhat forward." The entire tumor, together with an extension into the subpleural space, was bluntly dissected out. The patient seemed to do well for the first four days after operation but then developed hiccoughs and vomiting and died on his ninth postoperative day. Although a postmortem examination was not permitted except of the spinal wound, pathological examination of the tumor revealed a "round cell sarcoma."

About a year and a half later Dr. Abbe operated on a third patient who was thought to have a cord tumor. He was a 26 year old telegrapher who for five years had developed signs of a slowly progressive cord lesion in the midthoracic region. At operation, at the Post-Graduate Hospital in December 1891, instead of a cord tumor, the patient was found to have syringomyelia. The cord was greatly swollen over several segments by a cystic collection of clear fluid. "A drachm and a half" was aspirated through a hypodermic needle inserted through the posterior columns and the cord collapsed. There was no particular change in the patient's condition after operation. The case was presented before the Neurological Section of The New York Academy of Medicine by Dr. William B. Coley and Dr. Abbe on April 15, 1892.[6] This was the first recorded attempt at surgical treatment of a patient with syringomyelia.[7]

Although for many years he was not given credit for it, Dr. Abbe was the first surgeon to divide the posterior roots of the spinal nerves.[2-4, 8,9] The original idea was suggested, and the first suitable patient was referred to him, by Dr. Charles L. Dana. The patient was a 44 year old ice-man with severe pain involving the right arm and forearm. The pain had not been relieved by previous stretching of the posterior interosseous and ulnar nerves or by amputation of the arm. Because of the pain the patient was taking a half grain of morphine every hour.

At operation on December 31, 1888, under ether anesthesia, the right laminae of the lower four cervical vertebrae were removed and the dura exposed. No evidence of tumor or inflammation was found. The right sixth and seventh cervical nerves were exposed extradurally, were stimulated with an electric current and divided. The wound was packed open. The patient "bore the operation well but soon found

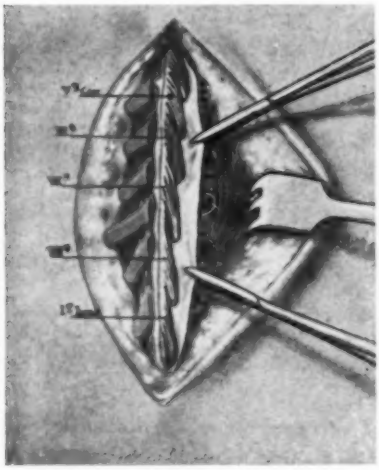

Fig. 1—An operative sketch of Dr. Abbe's showing the exposure for performing resection of the posterior roots of the brachial plexus. (St. Luke's Hospital Medical & Surgical Reports, 2:16, 1910. Reproduced by permission.)

Fig. 2—Sketch by Dr. Abbe of patient with multiple neurofibromata of the cervical sympathetic nerves. (Ann. Surg. 27:488, 1898. Reproduced by permission.)

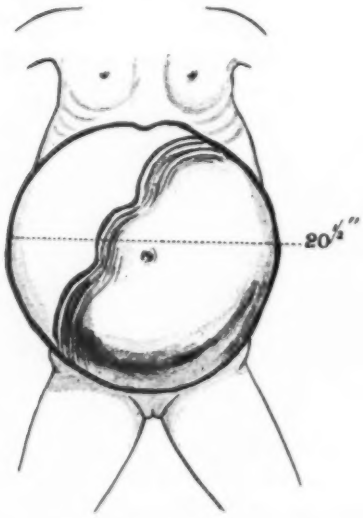


Fig. 3—Diagram of an infant with a large renal tumor removed by Dr. Abbe. (Ann. Surg. 31:273-385, 1899. Reproduced by permission.)

Fig. 4—Diagram of Dr. Abbe's string sawing method of dilating an esophageal stricture. (Medical Record, 43:225, Feb. 25, 1893: Medical Record, 72:890-892, 1907. Reproduced by permission.)

his old pain seemed much the same." Accordingly, forty-eight hours later, without anesthesia, the patient was placed prone "under a brilliant light," the packing removed "revealing a large clear dry wound at the bottom of which lay the dura throbbing and sound." The dura was slit open for one and a half inches "and was scarcely at all sensitive to cutting." The posterior root of the eighth cervical nerve was picked up intradurally and divided "close to the posterior columns of the cord" and a small piece was removed for "microscopical examination." "Handling this nerve root gave him the greatest pain." In addition the posterior root of the seventh cervical nerve, which had been previously divided extradurally, was also divided intradurally. The peripheral ends of the cut sixth, seventh, and eighth nerves were again stimulated with the electric current while careful observations of the responses were made by Dr. Dana. The dura "was sutured with fine catgut" and after injecting cocaine under the skin the entire wound was closed, leaving "a small linear scar." The patient "was allowed enough morphine to quiet the pain for eleven days," was then allowed to sit up and the drug was stopped entirely.

During the next few years Dr. Abbe and Dr. Dana were again able to repeat their observations and similar, but more extensive, posterior rhizotomies were performed on several more patients in one stage.[9] In 1911, in an article entitled "Resection of the posterior roots of the spinal nerves to relieve pain, pain reflex, athetosis and spastic paralysis—Dana's operation," Dr. Abbe[10] described the subsequent course of the first three patients who by then had been followed for 16 to 22 years and added two more cases not previously reported.

His interest in spinal surgery included other aspects also.[5, 11] He discussed the proper management of patients who became paraplegic following injury to the spine, particularly whether operation should be done or not, and recounted his own experience with decompressive laminectomy both good and bad.[12] He recommended the surgical repair of spina bifida with meningocele and condemned the earlier methods of injection.[13-15] He was interested in the treatment of Pott's disease of the spine and reported on his results with curetting out draining sinuses and infected bone.

During the latter part of the nineteenth century and the beginning of the twentieth a number of surgeons were seeking a satisfactory method for relieving the severe pain of trigeminal neuralgia. Early at-

tempts at section of the appropriate peripheral branches of the trigeminal nerve were found to be of only temporary benefit. Gradually operations were devised in which the larger branches were divided closer to the ganglion and eventually efforts were made to destroy or curette out the gasserian ganglion itself. Dr. Abbe's experience with the treatment of this condition was an extensive one and he presented a number of papers on the subject.[16-18] His early papers[19] reported his results with the best of the various peripheral nerve sections used up to that time. Although some patients appeared to have been cured by these methods there were recurrences and he was quick to adopt the newer operation devised by Dr. Frank Hartley of New York in 1891. In this the ganglion was exposed through a temporal intracranial extradural approach and the maxillary and mandibular nerves were divided intracranially at the foramina rotundum and ovale. Still concerned lest the nerves regenerate Dr. Abbe tried to prevent it by implanting a sheet of sterile gutta-percha rubber tissue over the foramina.[17, 20, 21] To test more fully whether such rubber tissue could be satisfactorily tolerated by the body he conducted a series of experiments on rabbits implanting the gutta-percha in various locations. He concluded that—"Its presence is borne well in any tissue. On the surface of the brain or between the dura and the skull, or outside the skull under the scalp, it maintains its full shape and remains unchanged. During five months before the rabbits were killed the rubber tissue laid on the surface of the brain without adhesions except at a portion of its margin."

In 1903 he reported the results of this work and the use of this method in eight patients followed for varying periods up to seven years.[17, 21] He believed that it was probably an effective aid in preventing regeneration of the nerves and safer than trying to remove or curette out the ganglion which almost always resulted in profuse hemorrhage and carried a relatively high mortality.

The idea of implanting rubber tissue was also used by Dr. Abbe in treating some patients with focal epilepsy due to cortical scars.[20, 22-25] After exposing the scarred area of the brain and dissecting the dura from it he placed the sheet of rubber over the brain and closed the dura over it. Some patients were improved after this was done but not always as he was to learn from Dr. McCosh[26] who, on re-exploring one of these cases, found the rubber all rolled up in a little ball embedded in the scar tissue. Dr. Abbe himself discovered much the same situation in some of

his patients whose tic douloureux recurred.[27]

From his service at the Roosevelt Hospital in 1897 he presented before the New York Surgical Society an interesting case of a nine year old girl with "large multiple neurofibromata of the cervical sympathetic."[28]

Two years later he related his experience, from this service, with the "Effects of intracerebral and subcutaneous administration of tetanic antitoxin in tetanus observed in nine cases."[29] Antitoxin was just beginning to be used and as with many new ideas Dr. Abbe was quick to learn about it, to study it and attempt to evaluate it. He concluded that the antitoxin was of distinct benefit and although the value of the intracerebral injection was not proven it was worthy of further trial in the most serious cases.

Throughout this same period when he wrote the papers already mentioned he was equally prolific on subjects of interest to the general surgeon. He wrote on intestinal obstruction,[30, 31] intestinal anastomosis and suturing,[32, 33] gallbladder disease,[34] and gallstone obstruction.[35] He discussed the problems of acute general peritonitis,[36, 37] peritonitis due to perforating typhoid ulcer[38-40] and peritonitis due to tuberculosis.[41-43] He made a special study of the cause of appendicitis,[44, 45] examining appendices removed during the "interval" between attacks.[46] On one occasion he presented three cases of large pancreatic cysts[47] which he had drained, and on another, two cases of intra-abdominal cysts arising from the kidney.[48]

The first major operations performed at the new Babies Hospital, then at Lexington Avenue and 55th Street, were done by Dr. Abbe.[49] There are two cases of particular interest on which Dr. Abbe operated. They were tremendous tumors of the kidney which filled the abdomen.[50, 51]

The first of these was a two year old girl with an abdominal mass increasing in size for five months. Operation had been refused at three of the largest hospitals in the city. Examination revealed the "abdomen to be distended by a solid growth occupying its greater portion, crowding upward and spreading the ribs, causing the lower abdomen to sag and fill the right loin." In the operation, which was performed on April 12, 1892, care was taken to wrap the patient warmly and she was positioned tilted at an angle of 45°. A transverse incision was used. There were numerous large veins over the surface of the tumor. "The growth

was shelled out of its bed and a good pedicle was formed which was tied with a silk ligature." There was little blood lost, "scarcely half an ounce." The operation lasted 45 minutes and "was well borne." The patient made a good recovery. The pathological report was round cell sarcoma but examination by Professor E. K. Dunham of Bellevue showed it to be "carcinoma sarcomatosum."

The second case was equally astonishing and was presented to the New York Surgical Society for examination. This patient was a girl one year and two months of age who was admitted to the Babies Hospital in 1892. The patient's mother had noted an enlargement of the abdomen for six weeks and examination revealed a solid tumor filling the abdomen. Operation was performed on November 20th, before a considerable audience. The same precautions were taken with this child to keep her warm and to place her in an inclined position. A transverse incision was again made. The mass was very large and covered with big veins. The greatest loss of blood occurred at the beginning of the operation on incising over the mass—about an ounce. After the incision the tumor was dissected out with the finger. A "narrow pedicle was at last made which was found to be double, one half holding the vascular supply of the tumor with its cellular bed and the other, when separated, holding the renal vessels and pelvis of the kidney. This was connected with a very pale kidney elongated to about five inches and throughout its entire length apparently normal in structure except that its upper end merged with the tumor with which it had been completely removed from its bed in the loin. Before ligating the double pedicle, critical examination showed that it was possible to amputate the kidney above its pelvis leaving one and a half inch of apparently sound structure attached to the tumor. This was done and a continuous suture of the kidney stump applied. The greater pedicle of the tumor alone was then ligated with silk and the kidney replaced in the loin. Not more than two ounces of blood were lost." The patient was kept inclined at 30° for two or three days after operation. Convalescence was smooth. The baby was fed on its mother's milk. The tumor weighed seven and one half pounds. The child, after operation, weighed only 15 pounds. The pathological report was rhabdomyosarcoma.

An excellent follow-up report on these patients was given in a paper presented before the 58th Annual Meeting of the Maine Medical Association at Bar Harbor in June 1910.[52]

The first case, the two year old girl, remained in perfect health until three and a half years after operation. The second case, with the tumor weighing seven and a half pounds and the patient weighing 15 pounds, had "grown to fine healthy womanhood and had already survived eighteen years with every prospect of continued health and vigor." It has subsequently been learned from one of the nurses who cared for Dr. Abbe shortly before he died that this remarkable patient later was married and had a child of her own and was still in good health as late as 1924.[53]

It would not be possible to review in any detail all of the many different surgical conditions about which Dr. Abbe wrote. There are perhaps one or two subjects that he was interested in which deserve additional comment. One of these is the ingenious method he devised of dealing with esophageal strictures following a burn of the esophagus from swallowed caustics or acids.[54-57]

In 1892 such a patient in whom it was not possible to pass a dilator down through the mouth, came under Dr. Abbe's care at St. Luke's Hospital, and on December 9th of that year he operated on the patient, performed an esophagotomy in the neck and tried to pass a bougie down through the stricture in the lower esophagus via this opening but unsuccessfully. He therefore proceeded to make a simple gastrostomy and, inserting his finger up through the stomach into the orifice of the esophagus in the cardiac end, he was able to guide a very small filiform bougie, to which he attached a piece of heavy braided silk, up past the stricture out through the opening in the neck. With the string as a guide he attempted to pass a next larger size bougie up through the stomach and esophagus from below but could not do so until by exerting pressure on the bougie and sawing with the string the bougie suddenly passed quite easily. He was able to pass three larger sized bougies in the same manner until the stricture was cut and dilated to almost the normal size of the esophagus. "Bleeding was practically insignificant." "Uninterrupted recovery ensued." After a week the same method of dilatation was repeated. After this it was possible to pass bougies from the mouth to the stomach without difficulty. The string was removed. The wound in the neck closed spontaneously. "The patient was allowed to eat everything." She had no difficulty in swallowing raw oysters, meat, vegetables as naturally as ever for the first time in four years. She gained four and a half pounds a week. Eight weeks postoperatively the gas-

trostomy opening was dissected out, inverted and closed.

A follow-up on this patient 15 years later was given in a subsequent paper.[58, 59] "Post-operatively the largest bougie was passed down the patient's esophagus, at first every few days, then once a week, and monthly during the latter half year. Since then once a year I have tested the esophagus and there has never been the least recurrence of stricture."

Later, for another patient treated by this method whose stricture started to re-form, Dr. Abbe "devised a dilating metal guide which carried a string down to the face of the stricture and back again, so that working entirely from the patient's mouth the stricture could be worn through on the same principle."

Special mention should be made of Dr. Abbe's contributions to the surgery of the other end of the gastrointestinal tract. In 1902 Dr. Abbe presented a paper to the American Surgical Association on "The abdominal route for approaching rectal tumors."[60] In this he pointed out the advantage of the abdominal or combined abdomino-perineal approach for lesions lying high in the rectum near, at, or above, the peritoneal cul-de-sac.

Dr. Abbe wrote the section on surgery of the rectum and anus in Keen's Surgery.[61] It is a chapter well worth reading, written by an obvious authority, and well illustrated with many excellent drawings and photographs. It covers the subject thoroughly from the most common lesions to the various types of curative and palliative resections for malignant tumors.

Time does not permit a discussion of Dr. Abbe's work in the field of vascular surgery but he wrote several papers on the subject. He tried to promote clotting in an aneurysm by inserting catgut and wire into it and passing an electric current through the wire.[62] He experimented in animals on a method for anastomosing arteries over a piece of glass tubing[63] and, later, adopted Matas' method of obliterating aneurysms by opening them and closing the mouth of the aneurysm from within the sac.[64, 65]

His contributions to the field of plastic surgery[66-79] have been well reviewed by Dr. Richard B. Stark.[80]

Probably Dr. Abbe's greatest interest lay in the treatment of neoplasms of all sorts.[81] For a time he was on the staff of the New York Cancer Hospital. He discussed the surgical treatment of tumors of the skin, lips, face, mouth, jaw, palate, tongue, breast, kidneys, gastro-

intestinal tract, abdominal wall, and extremities.

He had an extensive experience with carcinoma of the breast, having done several hundred operations for it.[82, 83] He felt that better results were to be expected with more extensive operations, advised wide excision of skin with removal of the pectoral muscles, the contents of the axilla, and of the supraclavicular nodes when extension seemed to be in that direction. He was one of the first to recognize the influence of the ovaries on breast carcinoma[84, 85] as originally pointed out by Beatson, and removed the ovaries in a number of patients with extensive metastatic carcinoma of the breast. He found that in a few, particularly in patients who were still menstruating, there was a remarkable regression of the disease, in some there seemed to be a transient arrest of the disease, and in many there was no effect whatsoever. He mentioned the effects of other endocrine glands on the growth of tumors.

Several of his papers stressed the role of tobacco in the production of cancer, particularly of the lips, mouth, tongue, and throat.[86-88]

It was from this great interest in malignant new growths that he became curious about radium and the effects of radioactive rays on tumor growth.[89-114]

After about 1897-1900 Dr. Abbe resigned most of his positions in the other hospitals of the city and concentrated on his work at St. Luke's Hospital.[115] By that time the hospital had moved from its original site on Fifth Avenue at 54th Street to its present location on Morningside Heights.

When he arrived at the hospital he was formally met at the front door by the surgical house staff who accompanied him on his rounds.[116] His rounds were devoted to teaching. On the days when Dr. Abbe was to operate there were often visitors, many of them prominent physicians and surgeons in the city, and others, visitors from abroad.[116] His cases were always done in the large amphitheater on the surgical floor of the hospital. He always scrubbed with Ivory Soap.[116] He was one of the first surgeons in New York to use rubber gloves[117] after their introduction into operating room technique and commented on their comfort, the feeling of security they gave the surgeon, and the protection they offered the hands from contamination and odors from abscesses and other lesions surgeons were prone to get their hands into. He usually wore glasses while operating.[116] They were soaked in alcohol for some hours before. After his scrub he would walk over to the basin of alcohol

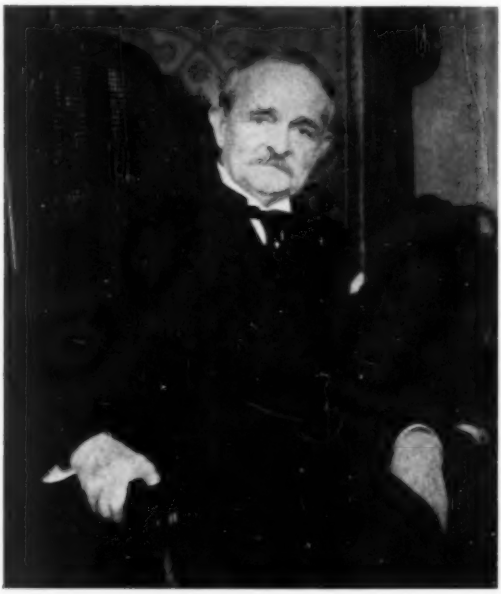

Fig. 5—Dr. Abbe in his later years. (Courtesy of Dr. and Mrs. Robert Abbe MacKenzie.)

in which the glasses were soaking, lift them out and put them on. At times during the operation he would readjust them without rescrubbing, to the consternation of some members of the staff.

During operations his manner was always one of outward calm and quiet.[118] He never raised his voice or became excited, even under the most trying circumstances. He seemed imperturbable. This atmosphere of calm pervaded the whole operating room staff. He always explained what he was doing to those around or to the visitors. He was dramatic, daring, and full of original ideas. He was deft and skillful in his work[119] and handled tissues with great gentleness. This was reflected in the generally excellent results he obtained.

The nurses at St. Luke's Hospital who still remember Dr. Abbe do so with the greatest admiration.[120] They remember him as a great gentleman. They remember the wonderful manner he had with patients, his insight and understanding. They remember him for his many kindnesses

to them. Every spring, for the graduation exercises in the training school, Dr. Abbe would send up as many American Beauty roses as there were nurses graduating. After his death Dr. Abbe left a fund of $10,000 to be used for the care of sick and needy nurses at St. Luke's Hospital.[121]

Evidently a facile speaker, Dr. Abbe belonged to many local, national, and international organizations. He was a member of the New York Clinical Society, the Practitioners Society, the New York Medical and Surgical Society, and the Charaka Club. He was an active member of The New York Academy of Medicine, where he gave a number of lectures and papers, and from 1906 to 1908 served as Vice-President.[122] There were innumerable meetings of the New York Surgical Society at which he presented cases, read papers, took part in the discussions or showed some interesting specimens, particularly during the years 1894 and 1895 when he was its President. He belonged to the College of Physicians of Philadelphia where he established the custodianship of the Rush, Jenner, Lister, Pasteur and Curie mementoes.[123, 124] He was a Fellow of the American Medical Association and the American College of Surgeons, and a member of the American Physicians and Surgeons Society, the American Surgical Society, the International Surgical Society and the Pathological Society. In addition to these professional organizations he belonged to the University Club and the Century Association.

About 1882, when the telephone was first beginning to be used in the city, he was one of the first doctors to have one installed in his office. It caused considerable comment and many inquiries from his friends.[125] Associated with him for about ten years, between 1890 and 1900, was Dr. Arthur Fisk whom Dr. Abbe referred to as his partner and with whom he shared his office.[126]

Dr. Abbe's office and instrument nurse for many years was Miss May Moon, a pleasant, efficient little English woman who devoted much of her life to Dr. Abbe's work.[127] It was still customary in those days for some operations to be done in the patient's home and on such occasions Miss Moon accompanied Dr. Abbe and set up, and helped him with, the operation.[126]

During the summer months Dr. and Mrs. Abbe often went to Bar Harbor, Maine. Here Dr. Abbe enjoyed himself in climbing the mountains, studying nature, taking photographs in both black and white

and in color, and painting water-colors. He bought a place in Bar Harbor called "Brook End," "where Duck Brook meets the Bay."[128] Having become an admirer of the Japanese and their art, following a trip to the west coast and Japan, he constructed a Japanese garden in this Maine setting with a small pond on which could be seen two swans, Pierre and Marie, named after his friends the Curies.

After Mrs. Abbe died he continued to spend much of his time in Maine. He made several beautiful papier maché relief maps of the Maine coast[129] in the vicinity of Bar Harbor and Mt. Desert. These were constructed of wet blotting paper and painted in shaded colors, using greens for the land and mountains, and blues for the sea. They were extremely detailed and accurate. In 1922 he noted[128] some Indian implements in a shop window in Bar Harbor and from this he began a new interest in the study of the Indian relics of the Red Paint people who once lived in this part of the Maine coast. He became a collector and an authority on the subject. He then conceived of establishing a museum for his maps and collections. He wrote others who had made collections of these Indian implements and asked if they would give them to the museum. One man, of whom he had made[130] such a request, refused to send his collection unless the building was fireproof. Dr. Abbe assured him that it would be and designed the building himself. The museum, now known as the Abbe Museum, is situated in the Glen of Sieur de Mont Spring in Acadia (formerly Lafayette) National Park in the northern part of Mt. Desert. In the great forest fire at Bar Harbor in 1946 the museum was in the path of the flames and it is a tribute to Dr. Abbe that it and all its contents survived unscathed.

During most of his early life Dr. Abbe enjoyed reasonably good health. In 1912, noticing a progressive enlargement of his head, he[131] suspected that he might have Paget's disease and this was subsequently confirmed with x-rays of his skull. In his later years, after the age of 60, he suffered from rather frequent attacks of anginal pain, dyspnea, and palpitations, but it was not until February 1924[132] that he was found to have a severe aplastic anemia probably resulting from his earlier exposure to radium rays. His hemoglobin at that time was only 35 per cent. With some reluctance he consented to have a transfusion and his anginal pain was greatly relieved. Thereafter he was given transfusions of 1000 cc. about every three weeks. These were given by Dr. Lester Unger,[133] of this city. His hemoglobin was kept around 60 to 65 per

cent. In July 1925, because of a severe attack of acute cystitis, he underwent a suprapubic cystotomy. He was kept alive with transfusions for a period of four years, receiving over 60 or 70 of them. During this time he was able to complete much of the work he was doing in building and setting up the museum at Bar Harbor. Shortly before it was opened to the public he died, on March 7, 1928, at the end of his 76th year.

At the dedication ceremonies of the Abbe Museum a few months later Bishop Lawrence quoted the following excerpt from one of Dr. Abbe's letters.[115, 130] "Conquest only comes from persistent climbing upward. Often it seems like the excitement I have felt when climbing Sargent or Green Mountain, or Fujiyama in Japan, the nearer one gets to the top the harder it seems – then all of a sudden one gets there. That glorious experience I have had many, many times in every field of adventure, in surgery, science, or climbing, and I like the game."

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# NEW YORK PATHOLOGICAL SOCIETY

## ABSTRACTS OF PAPERS AND DISCUSSION*

Presented at the Meeting, April 22, 1954, at The New York Academy of Medicine

## *Experimental Production of Carcinoma with Cigarette Tar*

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In view of the large scale clinical evidence associating smoking, particularly cigarettes, to lung cancer, experimental studies were begun to determine the carcinogenic effect of cigarette tar on the experimental animal. $CAF_1$ mice were painted with tobacco tar obtained in a manner simulating human smoking habits as closely and as practically as possible. Forty milligrams of tar were applied three times a week. The first cancer was observed at ten months. At the end of two years 59 per cent of the animals developed papillomas and 44 per cent carcinomas. None of the control animals painted with acetone, which was used as a solvent, developed any lesions.

It is emphasized that these data do not necessarily prove that smoking may cause cancer in man. We feel that the human data rest primarily on their own merit. The animal data chiefly serve as a tool to identify, isolate, and remove active carcinogenic fractions from tobacco tar. Combined chemical and biological experiments are now in progress to identify such materials.

## *Preliminary Studies on the Chemical Fractionation of Tobacco Tar*

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To provide cigarette smoke for fractionation work which is designed to isolate the compound (or compounds) responsible for the production of cancer in mice[1] a smoking machine has been constructed which accommodates 240 cigarettes at a time and which simulates human smoking habits by taking a two-second puff of 35 to 40 ml. volume at 58-second intervals. The smoke is collected in liquid air-cooled traps, and the condensate ("tar") is removed therefrom with the aid of acetone.

In our fractionation procedure the tar-acetone mixture is distilled to remove the solvent and low-boiling tar components, and is then extracted with hydrochloric acid to remove the water-soluble and basic compounds (AB). Further steps include a vacuum distillation (distillate-EA), extraction of the residue with petroleum ether (residue-J), and equilibration of the extract with aqueous methanol (methanol layer-K, ligroin layer-M).

In a typical run, fraction AB represented 26 per cent, EA 5 per cent, J 23 per cent, K 6 per cent, and M 23 per cent of the starting tar. Some of the properties of the several cuts were presented.

*REFERENCE*

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# *Sebaceous Gland Activity as a Measure of the Relative Carcinogenicity of Certain Oils and Tars*

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The present paper describes histologic studies made upon the skin of mice within a few days after application of materials of varying carcinogenic potency. These studies revealed that the number of active sebaceous glands per centimeter were inversely related to the relative carcinogenic potency of test materials.

The materials were applied with a brush to the midline of the back. Four days later the animals were sacrificed and a strip of skin was removed from the treated area. Sections were made and stained with hematoxylin and eosin.

In control animals or in animals painted merely with a solvent such as acetone, benzene, chloroform or U. S. P. white mineral oil, or with non-carcinogenic compounds such as phenanthrene, fluoranthene or pyrene, the sebaceous glands were distended by the characteristic foamy, sebum-filled cells that they produce. In animals painted with solutions of the powerful carcinogens, methylcholanthrene, benzpyrene, dibenzanthracene or 9,10-dimethyl-1.2 benzanthracene, the sebaceous glands were empty or indistinguishable.

A series of petroleum derivatives, shown in this laboratory to produce skin tumors in mice[1] after prolonged applications were tested for their early effects upon mouse skin. Some of these samples injured the skin severely, and observations for a selective effect upon the sebaceous glands could not be made in the presence of severe dermatitis. This difficulty was overcome by limiting the number of applications or by

TABLE I—SEBACEOUS GLAND COUNTS FOUR DAYS AFTER SINGLE APPLICATION OF FRACTIONS DISTILLED FROM A CATALYTICALLY CRACKED OIL

| *Sample No.* | *Boiling Range* | *CI/TI* | *Number of Sebaceous Glands per CM.* | |
|---|---|---|---|---|
| 404 | 600-650°F. | 0/0 | 15.0 | 13.0 |
| | | | 14.5 | 10.5 |
| | | | 8.0 | 6.5 |
| | | | 6.5 | 6.0 |
| 406 | 700-750°F. | 0/30 | 5.0 | 4.0 |
| | | | 3.0 | 1.5 |
| | | | 1.0 | 0.5 |
| | | | 1.0 | 0 |
| 408 | 800-900°F. | 14/36 | 3.5 | 1.5 |
| | | | 2.5 | 2.0 |
| | | | 1.5 | 0.5 |
| | | | 0 | 0 |
| 409 | 900-930°F. | 17/50 | 1.0 | 0.5 |
| | | | 0 | 0 |
| | | | 0 | 0 |
| | | | 0 | 0 |

N.B. CI/TI Cancer Index/Tumor Index. These are measures of carcinogenicity determined in prior long-term tests.

Cancer Index is the number of animals that developed cancer divided by the number of animals in the test group less any dead before 90 days without cancer.

Tumor Index is the number of animals that developed tumors (papillomas and cancers) divided by the number of animals in the test group less any dead before 90 days without tumors.

Each sample was painted on four mice and counts made on two slices of skin from each mouse.

TABLE II—SEBACEOUS GLAND COUNTS AFTER FOUR DAILY APPLICATIONS OF 5 PER CENT SOLUTIONS IN ACETONE OF FRACTIONS DISTILLED FROM A STEAM-CRACKED PETROLEUM TAR

| *Sample No.* | *Boiling Range* | *CI/TI* | *Number of Sebaceous Glands per CM.* | |
|---|---|---|---|---|
| 393 | IBP-600°F. | 0/4 | 6.7 | 5.2 |
| | | | 5.5 | 2.8 |
| | | | 4.4 | 3.9 |
| 394 | 600-650°F. | 0/10 | 3.5 | 1.2 |
| | | | 0.6 | 0.6 |
| | | | 0.6 | 0. |
| 397 | 750-800°F. | 33/74 | 0 | 0 |
| | | | 0 | 0 |
| | | | 0 | 0 |

TABLE III—SEBACEOUS GLAND COUNTS AFTER FOUR DAILY PAINTINGS WITH ACETONE SOLUTIONS OF CIGARETTE SMOKE CONDENSATES AND FRACTIONS THEREOF

| *Sample* | *Material* | *Conc.* | *Sebaceous Glands* |
|---|---|---|---|
| | | | *per cm.* |
| B | Total condensate after distillation (65°C. 760 mm.) | 50% | 0<br>0<br>0<br>0<br>0.3 |
| B | ditto | 20% | 0.3<br>0.8<br>0.8<br>0.8<br>3.3 |
| B | ditto | 5% | 1.8<br>5.0<br>5.5<br>8.5<br>10.6 |
| D | Acid-washed B | 50% | 0<br>0<br>0<br>0.3<br>0.3 |
| EA | Distillate from D (85°C. 1 mm) | 50% | 10.<br>13.3<br>17.<br>24.3<br>28.1 |
| F | Residue from D after removal of EA | 50% | 0<br>0<br>0<br>0<br>0.5 |

resorting to dilutions. Table I shows results observed four days after a single application of fractions distilled from a high-boiling, catalytically cracked oil. Table II gives results found after four daily applications of acetone dilutions of a tar. In each case it can be seen that the sebaceous glands were less numerous in proportion to the increasing carcinogenicity of the samples. In comparison with the findings presented in the tables, it may be noted that the number of sebaceous glands per centimeter observed after four daily applications of acetone alone ranged from 10 to 20.

As in the case of the petroleum derivatives, a similar inverse relationship with the relative carcinogenicity of five coal-tar derivatives was observed in further tests.

Tests of this nature have been conducted with cigarette smoke condensates and fractions thereof provided by Dr. Alvin Kosak and his associates. Results, presented in Table III, show that the total condensate applied at 50 per cent concentration in acetone caused complete suppression of glands. A similar result was obtained with the residue after removal of materials soluble in acidified water. A distillate prepared at reduced pressure caused no diminution in the number of sebaceous glands, but the residue remaining after this distillation had an effect comparable to that of the original total condensate. These findings suggest that observations upon sebaceous glands may provide a rapid means for tracing the as-yet unknown compound(s) in cigarette smoke condensates that have the property of inducing tumors after long-continued application to the skins of mice or rabbits.

Long-term tests for actual tumor induction by those and other fractions of cigarette smoke are being conducted by repeated applications of these materials to mouse skin throughout the lives of the test animals. Until these tests are completed, the significance of the observations upon early changes in the sebaceous glands induced by cigarette smoke fractions cannot be evaluated.

*REFERENCE*

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# *Early Cytologic Changes Produced by Carcinogens*

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Dr. Smith has discussed the reasons for our laboratory's endeavor to find a rapid screening test for carcinogenic activity. Early in the course of this project, it was observed that, after four daily paintings with a known carcinogen, mouse epidermal cell nucleoli had become strikingly enlarged. This phenomenon had been observed previously with pure chemical carcinogens. In 1938 Page[1] reported nucleolar enlargement in mouse skin beginning two days after the start of painting with methylcholanthrene and cholanthrene: the increase in size reached a maximum at seven days. Pullinger[2] in 1940 mentioned nucleolar enlargement three days after a single application of methylcholanthrene. Cowdry and Paletta[3] in 1941 noted increased nucleolar size after several weeks of painting mice with methylcholanthrene; they were not impressed with early changes.

It was obviously desirable to determine whether or not early nucleolar enlargement is a consistent and specific indication of carcinogenicity under the conditions of our experiments. Therefore a number of substances which were known to be carcinogenic in the dosage used were painted on the skin of mice. The materials used included carcinogenic fractions derived from petroleum, and pure chemical carcinogens, as well as cigarette smoke condensate and several fractions prepared from it by Dr. Kosak. In addition, non-carcinogenic irritants and several non-carcinogenic analogues of pure chemical carcinogens were painted in a similar manner.

Test substances were painted on the backs of $CAF_1$ albino mice on each of four consecutive days. The mice were sacrificed on the fourth day; midline longitudinal sections from the interscapular region were fixed in Zenker's solution with 5 per cent acetic acid for two or three hours. The sections were imbedded in paraffin and stained with hematoxylin and eosin. In most cases, skin strips about 2 cm. long from each of three or four mice were examined for each sample. Slides were examined as unknowns in every instance. In the first phase of this work, evaluations of nucleolar size were made by simple observation, without attempting quantitative measurement.

It was found that several non-carcinogenic substances caused some degree of nucleolar enlargement. The greatest change in this group was produced by a sample of U. S. P. white mineral oil; this sample had previously been tested in this laboratory and had produced no tumors in mice. After this observation was made, all of the test sections were re-evaluated, using the mineral-oil slides as a base line; only those materials which produced greater nucleolar enlargement than did the mineral oil were recorded as positive.

With these criteria no false positives have so far been obtained among the test substances whose carcinogenic potency is known; 3-methyl benzo (c) phenanthrene, which is a weak carcinogen, was the only material in this group falsely interpreted as negative. Cigarette smoke condensate, which has been shown to be carcinogenic for mouse skin, was one of the materials tested. It produced clear-cut nucleolar enlargement. Certain of the products of fractionation of the tar were also positive; these and the negative fractions are now being given long-term tests for carcinogenicity.

The high correlation of this indicator with known carcinogenicity in the mouse suggested trial of the method in other species. Material from laboratory animals other than mice has been prepared but has not yet been evaluated. In addition, the skin of a human volunteer has been painted with

several test substances.

The materials were painted daily for four consecutive days on one square centimeter areas of the upper back. On the sixth day punch biopsy specimens 5 mm. in diameter were taken from each test area and from an untreated control area. Up to this time no gross changes had been observed in the painted areas. Sections were fixed and prepared in the same way as in the case of mouse skin, except that the human tissue was serially sectioned.

The materials painted included a 0.5 per cent solution of 3-4 benzpyrene in acetone; 50 per cent coal tar in acetone; a petroleum derivative which is highly carcinogenic for mice, rabbits, and monkeys; a 50 per cent solution of turpentine in acetone; U. S. P. white mineral oil; and a 50 per cent solution of cigarette-smoke condensate in acetone. All of these substances produced more or less epidermal hyperplasia; most of them also caused some degree of dermal or epidermal inflammation, or both. These factors showed no correlation with known or suspected carcinogenicity. Increase in size of nucleoli, however, did show such correlation.

The area painted with U. S. P. mineral oil showed only minimal nucleolar enlargement as compared with the untreated area. The cigarette-smoke condensate produced definite nucleolar enlargement. A greater degree of enlargement was found in the coal-tar treated area. This is particularly interesting because of the generally accepted ability of this material to cause cancer in human skin. The carcinogenic (for mice) petroleum derivative caused even more marked increase in nucleolar size. Benzpyrene produced the greatest degree of nucleolar enlargement. This material is highly carcinogenic for mice, but long-term tests have not been done on human skin.

Turpentine, which is not carcinogenic for mice and is not thought to be so for human skin, produced nucleolar enlargement only slightly less in degree than that resulting from tobacco tar. We do not know the significance of this finding, but it appears to be analogous to the situation in mouse skin in regard to U. S. P. mineral oil. In that instance, further observations indicated a distinct difference in degree between that enlargement and the change produced by carcinogens. Further tests on human skin with a larger variety of materials will be necessary to resolve this point in man.

These observations indicate that early increase in nucleolar size is sufficiently correlated with carcinogenicity of test substances in mice to provide another practicable screening test for use as a preliminary guide in fractionation of carcinogenic materials. In addition, the findings were of particular interest to us because of the well-known increase in nucleolar size which characterizes many fully developed malignant tumors. It is, of course, true that nucleoli are enlarged in some other situations in which cellular metabolism is high, as, for example, in some embryonic tissues. At present we are trying to develop a practical quantitative technique for measuring nucleoli. In addition, new materials and other species are being tested.

The early changes in human epidermal nucleoli afford the hope of providing an indicator for the carcinogenicity of substances for man. It should be emphasized that, with the exception of coal tar, none of the substances employed has been demonstrated actually to produce cancer in human skin.

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## *DISCUSSION*

CURTIS M. FLORY: The papers presented tonight have been of much interest to me. Some 15 years ago[1] I worked on this problem at the University of Chicago, but failed to obtain the extremely significant results presented here tonight. The paper of Dr. Wynder is of importance. He has obtained a high incidence of carcinoma in mice treated with tobacco tars and seems to have proven that tobacco tar is carcino-

genic for the skin of these animals. In previous studies on this subject most workers have obtained perhaps one or two carcinomas in a large number of mice painted with such substances. Occasional papillomas were more frequent, but at the end of such work there has always existed a certain amount of doubt as to whether tobacco tar is a definitely carcinogenic substance.

However, I would like to mention that work with rabbits gives one a different impression of the tumor-producing ability of tobacco tars. In these animals such substances may actually produce more papillomas than either coal tar or benzpyrene. Relatively few carcinomas are obtained. Roffo[2] has done a great deal of work with rabbits, and some with mice, on the subject of carcinogenicity of tobacco tars. His work is basic and must be referred to by those interested in this subject.

The studies of fractionation of tobacco tars reported tonight give us some hope that the actual carcinogenic substance may eventually be isolated. Even if it is isolated, however, it is very difficult to see how it may be kept from the lungs of cigarette smokers. Filters will probably not be too effective and it may be that we will go back to Turkish water pipes.

It is unfortunate that one cannot produce tobacco tars in large quantities by smoking cigarettes in the laboratory. If one could, work such as has been described tonight would be much easier.

DR. RAPPAPORT: How does the production of carcinoma in endothelial tissues compare with that in squamous cell tissues? In human carcinoma we do not find an increase around the mouth or trachea. I think the increase has been from the carina on down. I wonder if experiments were done on the production of carcinoma in endothelial tissue as well as epithelial.

ERNEST L. WYNDER: That is one of the most difficult questions. In clinical studies that we are now undertaking we find cancer of the tongue, of the buccal mucosa, of the mouth and larynx also to be associated with tobacco smoking. In these areas, however, additional factors have to be considered which do not seem to apply to carcinoma of the lung. These involve particularly heavy intake of alcohol and dietary deficiencies.The bronchial epithelium seems particularly susceptible to injury from the smoke, perhaps on a physical basis. The smoke is more easily trapped and accumulates in a smaller tissue space.

I should like to comment on the remarks made by Dr. Flory. In these brief reports we did not have occasion to go into the previous literature. In the field of tobacco tar Dr. Flory wrote an excellent paper.[1] It is easy to review the literature and to pick from each of the previous investigators the best findings from their particular experiments, so that it is much easier for a young investigator, on the basis of the experience of the older investigators, to undertake an experiment with perhaps somewhat more positive results. The young investigator thus owes a great deal to all the previous investigators.

MARTIN FRIEDRICH: In 1951 Dr. Sugiura[3] reported his work with butter yellow in which rats developed malignant hemangiomas and cholangiomas. He was able to confer 100 per cent protection against these tumors by simultaneously feeding his animals with 10 per cent liver or 15 per cent brewers' yeast. He also referred to the experiments of many others in which other foods, such as casein, fortified with riboflavin, kidney, whole wheat and other foods especially rich in B-complex factors also prevented the development of malignancies, following the administration of carcinogens. I wonder whether any work along these lines was done.

ERNEST L. WYNDER: This refers again to the study of dietary deficiency. To my knowledge such studies have not been done in animals. We have been very interested in dietary deficiencies, particularly vitamin B, iron, and riboflavin deficiencies, in cancer in man. This problem is being investigated in Sweden where a group of women seems to be deficient in iron, and possibly also in riboflavin. They have a high incidence of carcinoma of the tongue, buccal mucosa and hypopharynx. These women

do not smoke and are not heavy drinkers. We believe dietary deficiencies do play a role in certain cancers in man. It may be that this holds true in cancer of the tongue and hypopharynx, as well as cancer of the liver. It is interesting that iron and riboflavin both seem to play a role in cellular oxidation, riboflavin through the yellow enzyme, and iron through the cytochrome system. It is also interesting to observe that the clinical syndromes described in deficiencies of iron and riboflavin are somewhat similar. We believe that in these types of cancer these deficiencies play a significant role. It would be of great interest to reproduce these types of deficiencies in experimental animals. This is difficult because as far as iron is concerned it is hard to produce a chronic deficiency in the mouse or rat and to keep the animals alive long enough to do a long-term study.

CHARLES T. OLCOTT: What happens to the sebaceous glands that you do not see any more?

WILLIAM E. SMITH: Within a few days after application of a carcinogen, the sebaceous glands are no longer distended by their characteristic large foamy cells, but their thin-walled sacs can occasionally be identified. Later, they may again come to contain sebum-filled cells. For these reasons, I think we are not observing a destruction of the glands, but rather a temporary inhibition of their physiologic activity.

In answer to Dr. Rappaport's question as to differences in response of a tissue such as skin in comparison to a mucosal surface, I recall that Dr. Sugiura induced tumors on monkey skin by long-repeated application of a petroleum derivative. This same material failed to induce tumors when applied to the vagina. We must certainly take into account the differences between skin and the mucosa of the respiratory tract. For example, the bronchial epithelium is washed by a watery fluid, and we know very little about the effects of carcinogens applied to that surface.

MARVIN KUSCHNER: We have been working on the assumption that everyone would be happier if we could take these suspected substances and produce lung tumors rather than skin cancers. The problem has been that few people have, with any consistency, been able to produce a tumor in animals comparable to human bronchogenic carcinoma. Most of the experiments in this field have dealt with the production of adenoma in mice, a spontaneous tumor whose incidence can be affected by a variety of substances.

We have been engaged in exposing the bronchial epithelium of mice and rabbits to known carcinogens, particularly methylcholanthrene. We hope to extend the investigation to other species and other substances. It has been difficult to achieve any good-sized dosing of bronchial mucosa and at the same time keep animals alive for an extended period.

The difference in response of tissues such as bronchial mucosa, skin, and the vagina, as Dr. Smith indicated, may not be a fundamental difference. It may perhaps reflect a difference in achieving local persistence of carcinogenic material. In the skin, the hydrocarbons go into solution in the sebaceous glands and remain there for some time. Our own impression is that methylcholanthrene is cleared from the lung at a fairly rapid rate and we have seen it disappear in 24 hours. One of the problems, then, in induction of lung tumors would appear to be the achievement of adequate dosage levels by prolonging exposure.

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NEW YORK PATHOLOGICAL SOCIETY — continued

## *Abstracts of Papers and Discussion**

Presented at the Meeting, December 21, 1954, at The New York Academy of Medicine

# *Histochemical or Histological Techniques?*

J. B. LONGLEY

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Histochemistry, as it concerns staining methods, is not a mature discipline. It functions in its present state only because its component techniques can be put to use independently of one another. Here it differs markedly from electron microscopy and autoradiography, which are employed with all their subsidiary techniques or not at all. Whereas it is impossible to consider electron microscopy and autoradiography except as wholes, attention is readily diverted in the case of histochemistry to the individual methods, no one of which can represent histochemistry as a whole. This tendency is abetted by the natural and necessary preoccupation of histochemists at this stage of the development of their discipline with the development and evaluation of methods, rather than with general considerations or applications.

We may profit by the broader viewpoint to be obtained by considering a question such as the relationship between histologic and histochemical techniques. It is obvious that there are certain similarities between such techniques and also certain differences. If we look no farther than the techniques themselves, the relationship between them seems to be like that between peas and beans, similar, yet distinct.

But the real relationship of histochemistry to histology is something else. Probably little exception can be taken to the following as a definition of histochemistry: "Histochemistry is concerned with the chemical structure of the cells and tissues of living organisms and with the relationship of their chemical structure to function." If the use of the modifier "chemical" is dropped from this definition, there is left almost verbatim the definition of histology given by Maximow and Bloom: "Histology is concerned with the structural characteristics of the cells and tissues of living organisms and with the relationships of their structure to function."[1] Histochemistry, then, is not something that exists alongside histology, or overlapping histology, but something entirely contained within histology. And every histochemical technique must necessarily be also a histologic technique.

It is therefore incorrect to oppose histochemical and histologic techniques. The true alternative of histochemical, or "rational" histologic methods, is "classical" or empirical methods. And between these there is no unbridgeable gap, but a direct line of communication over which as the classical methods are rationalized they move to the histochemical side. We may hope that the only histologic staining methods in time will be histochemical ones, a development which will greatly enrich, and not impoverish, histology.

Since the fundamental difference between rational and empirical methods is not a matter of technique, it is not surprising that no technical criterion perfectly distinguishes

* Manuscripts received July 1955.

between these two types. Nevertheless there is one characteristic which is almost always found in the former which is relatively rare in the latter, namely the inclusion in the technical procedure of non-color producing intermediate procedures. A consideration of this characteristic can contribute much to our awareness of both the problems and the possibilities of rational methods.

The possible range of these procedures is very great, and they are the most flexible part of the histochemical armamentarium. Intermediate procedures are very often undertaken with the idea of making some final color reaction possible, but equally important is their application where it is intended to produce negative results, for instance as in digestion, blockade, or inactivation.

They are the means of increasing the usefulness of the all too few histochemical color reactions. The Schiff aldehyde reaction may be taken as a familiar example. Without the use of intermediate procedures, little but rodent elastic tissue would ever be seen by means of Schiff's reagent. But by the intermediate use of periodic acid it can be made to show the distribution of vic-glycols, by the use of peracetic acid to show unsaturated linkages, and so forth.

Through these procedures not only may the groups necessary for final color reactions be produced, but their identities or those of their precursors confirmed. If one questions whether in a given instance a periodic acid Schiff positive material contains vic-glycols (or perhaps $\alpha$-amino-alcohols) the demonstration of the blocking of the reaction by prior acetylation and its restoration by deacetylation is a very reassuring answer in the affirmative.[2]

But not only do such procedures permit refinements in the use of rational color reactions but in all probability they will play a leading part in the rationalization of the conventional empirical methods. To take a simple example, it can be shown by deamination of tissue sections that the conventional eosin stain is in general simply a method for staining amine groups. Eosinophilia, except in the granules of eosinophil leukocytes, is destroyed by this treatment.[3] A general rationalization of empirical staining methods along these lines would be the equivalent of converting the voluminous literature of descriptive histology into histochemistry, a tremendous free accession of knowledge.

What about the practical applications of histochemistry? Its methods may be used in exactly the same way as other histologic methods to make structures readily visible which otherwise might be invisible. An example of this principle, familiar to the pathologist, is the use of the periodic acid Schiff reaction for the demonstration of basement membranes and parasitic fungi.[4] A less familiar example may be the demonstration that in most vertebrates the proximal tubule of the kidney can be sharply divided into two, and so far only two, distinct parts,[5] either on the basis of the periodic acid Schiff reaction, or by one or more of a considerable number of enzyme methods.

But the special advantage of these methods is not made use of in such applications. Function in a living organism has generally two aspects, physical and chemical. Physical function is determined by the shape and arrangement of things, and chemical function by what these things are made of. Traditional histology, by the nature of its methods, has been confined almost exclusively to the study of shape and arrangement, and hence has been able to relate its findings only to mechanical function.

Recent applications of histochemical methods to the study of the kidney seem particularly good examples of how they are beginning to change this situation. The interesting, if unfinished, story of the action of mercurial diuretics on histochemically demonstrable succinic dehydrogenase is well known.[6, 7] The latest development in our own laboratory is the discovery of precise and definite changes in the distribution of histochemical materials in the renal tubules which are not completed till a long time after birth.[8] These are quite apart from and far more striking than any purely structural changes that can be discerned in the maturing kidney. They may well be the changes which have been sought to account for the changes in renal function which occur in young animals, which evidently must rest on a chemical or metabolic basis, rather than on a mechanical one.

Through histochemistry the pathologist

and histologist are beginning to enjoy a unique opportunity to study both the structural and chemical elements of function.

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*DISCUSSION*

MAX WACHSTEIN: I would like to ask Dr. Longley a question concerning the beautiful sections of the mouse kidney which he has shown. Would he say that the marked difference in the staining intensity of alkaline phosphatase in the terminal portion of the convoluted tubules is a phenomenon that is observed in all mammalian kidneys? In the rat these portions of the nephron apparently stain much more distinctly than in the sections from the mouse shown today. I would like to point out that the mouse kidney is different in certain histochemical reactions from other species. It shows, for instance, 5-nucleotidase activity in the glomeruli which is almost absent in the kidneys of other species under normal conditions.

J. B. LONGLEY: There is a general distinction between the upper and lower parts of the proximal tubule, but it cannot always be demonstrated on the basis of the periodic acid Schiff reaction. In species other than the mouse, it is usually easier to demonstrate this division with enzyme methods.

There is a considerable number of neglected anatomic observations which show the same thing. For example, it has been reported for a number of species that the cells of roughly the straight part of the proximal tubule have straight outlines, but in the convoluted part they are complexly interdigitated. In the cat and dog these portions are further distinguished by the presence or absence of fat. The cat has fat only in the upper part of the tubule, the dog only in the lower part.

Over a wide range of animals, the only one I have found so far in which I have not been able to satisfy myself of the duality of the proximal tubule is the frog.

# *Application of Electron Microscopy to Pathology**

JEROME GROSS

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The electron microscope may be applied to pathologic problems in several ways. The most obvious—and popular—is the histologic approach which until the recent development of ultra-thin sectioning has been the most difficult. It is possible by modern technique to study the macro-molecular organization of cells and tissue components in fixed and embedded serial sections of the order of 100 A in thickness. However, the great advantage of high resolving power brings with it serious problems. Adequate statistical sampling is difficult. One hundred sections 0.1$\mu$ thick represent less than .005 cmm. of tissue, and in addition, three dimensional evaluation will often require much of this small sample to be serially sectioned. A second problem is the identification of very small objects which have no distinctive morphology, such as round or irregular particles or non-striated fibers and filaments. Correlative studies, by analytical, physical-chemical and electron microscopic technique, of purified preparations obtained from tissues by fractionation will aid greatly in morphologic identification of such objects in the intact tissue. In pathologic material the presence of products of inflammation will probably interfere with identification. A third problem, the need for increased contrast of very small objects of low electron density, awaits the development of specific "electron stains."

Another approach to pathologic problems requires the production of morphologic alterations in well characterized tissue components by simple procedures which will allow as far as possible an interpretation of the action of the agent in producing the change, and also permit a determination of the range and specificity of morphologic alterations under the influence of a variety of known agents. With this knowledge it may be possible to predict the type of agent responsible for a particular structural abnormality in certain pathologic states. A study of the morphologic reactivity of collagen to acids, alkalis, detergents, swelling agents, and enzymes is an example.

The electron microscope has been most effectively used in this laboratory as one tool in a multi-discipline approach to the mechanism of fibrogenesis of collagen, a process of considerable importance in growth, healing and pathologic sclerosis. Collagen has an identifying finger print in the colloidal range of dimensions, namely a fiber axis period of about 640 A and a distinctive pattern of intra-period fine structure. This characteristic has made it possible to study the formation of fibrils from solutions of collagen and to characterize the fundamental building block of the fibril. Electron microscopic studies led to the discovery of soluble collagen in neutral salt extracts of connective tissue and to the method of converting the dissolved collagen, which appears to be a precursor, into typical cross-striated fibrils. Studies on the metabolic activity of this collagen fraction with labelled amino acids, physical-chemical characterization of the unit particle, certain amino acid and carbohydrate analysis of the extracted material in scorbutic and protein-deficient animals are at this stage more important than electron microscopy, which is now used primarily to check fibril-forming properties of the various extracts. The electron microscope is subordinated to the problem, not vice versa.

The effectiveness of this tool is greatly enhanced when morphologic information ob-

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tained thereby can be correlated and integrated with other structural, chemical and physiologic data obtained on the same material.

*DISCUSSION*

EDITH E. SPROUL: I should like to ask Dr. Gross a question. I am not sure it is a fair one. The ordinary staining techniques leave considerable question concerning the relationship between collagen and reticulin, and I wonder whether electron microscopic studies may have anything to contribute to that.

JEROME GROSS: We studied this question some time ago by examining the collagen fibrils of the rat skin. In the newborn rat practically all the collagen fibers are argentophilic; as the animal gets older, fewer stain with silver, and more stain with the usual collagen stain. Under the electron microscope the fibrils of the newborn rat skin show the usual 640 A. axial period. As the animal gets older, there are increasing numbers of thicker fibrils, and as he grows into maturity there are still thicker ones. As far as I can tell, they are all typical of collagen.

ALFRED ANGRIST: The photograph of the kidneys which Dr. Gross showed seemed to show a central halo in the basement membrane of the glomerulus, and I wonder whether it is definitely established that this is a unique type of membrane composed of several layers. Have you combined electron microscopic studies of the membrane with the x-ray-density studies of these areas?

JEROME GROSS: I just showed those slides to illustrate the type of electron microscopic histology that is being done. I do not know the details of the basement membrane. I do know that this is not characteristic of all basement membrane. Dr. Fawcett, who made these preparations and took the beautiful electron micrographs, tells me the basement membrane looks more or less amorphous, does not seem to show too much differentiation, and is tremendously varied, whereas Weiss's study of the basement membrane of the skin shows very beautifully the quilt-like network of fibrils. There are basement membranes and basement membranes.

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## *The Application of Radioactive Tracer Techniques to Problems in Pathology*

PATRICK J. FITZGERALD

Department of Pathology, State University of New York, College of Medicine at New York City, Brooklyn, N. Y.

A complete summary of this work appears in the following articles:

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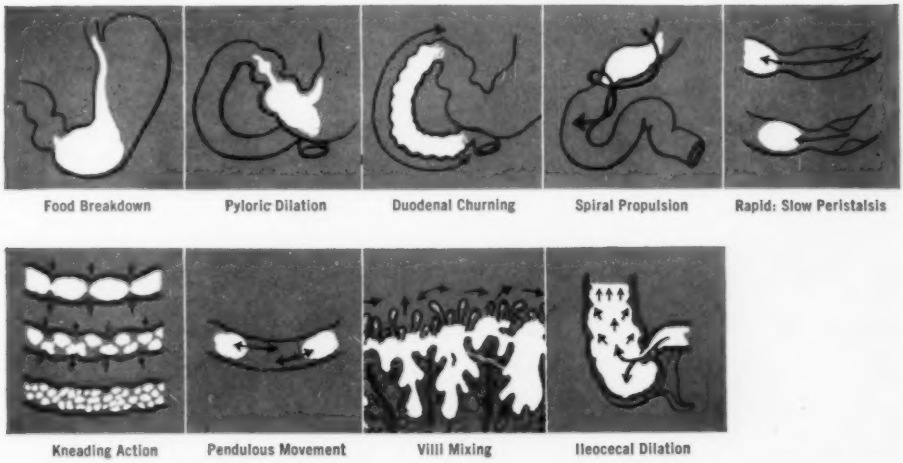


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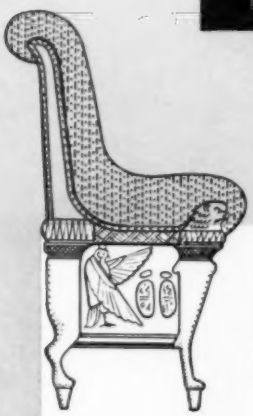

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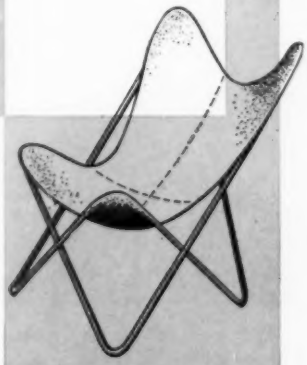

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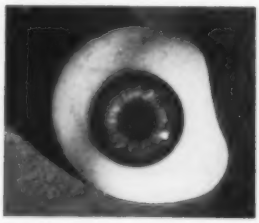

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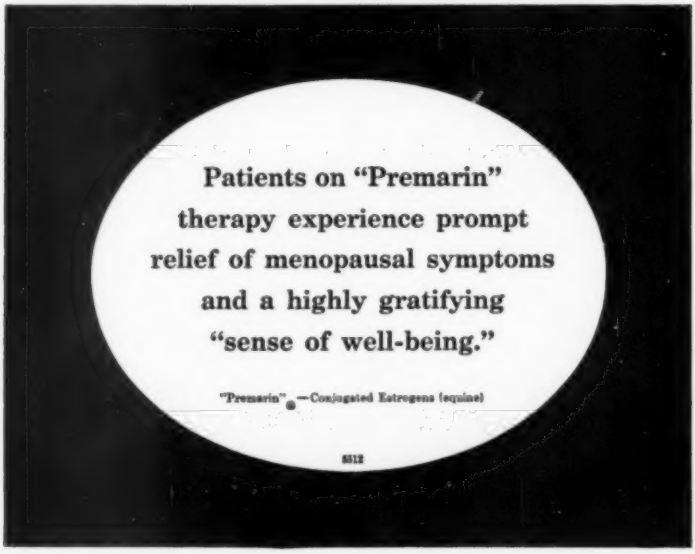


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**JANUARY 19** CANCER OF THE LUNG — William L. Watson, *Attending Surgeon, Memorial Center, New York.*

PYOGENIC INFECTIONS OF THE SKIN — Frank C. Combes, *Professor of Dermatology and Syphilology, New York University Post-Graduate Medical School, New York.*

**JANUARY 26** THE EPIDEMIOLOGY OF HEMOLYTIC STREPTOCOCCAL INFECTIONS — C. H. Rammelkamp, *Professor of Medicine, Western Reserve University, Cleveland, Ohio.*

THE PRESENT STATUS OF SYPHILIS — Charles R. Rein, *Associate Professor of Clinical Dermatology and Syphilology, New York University Post-Graduate Medical School, New York.*

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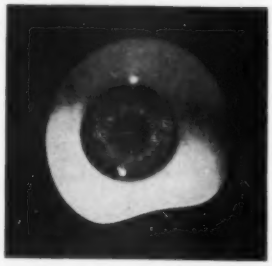

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1. J.A.M.A. 159:645 (Oct. 15) 1955.
2. J.A.M.A. 158:386 (June 4) 1955.

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